# WEST Search History

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| | *DB=PGPB,USPT,JPAB,DWPI; PLUR=YES; OP=ADJ* | | |
| ☐ | L7 | L6 and @pd > 20041224 | 9 |
| ☐ | L6 | lox71 or lox66 or lox2272 or lox511 | 49 |
| ☐ | L5 | L3 and L4 | 11 |
| ☐ | L4 | (lox P or loxP) near3 (mutat$ or alter$) | 107 |
| ☐ | L3 | trap$ near3 vector$ | 1245 |
| ☐ | L2 | lox66 and loxp | 22 |
| ☐ | L1 | lox66 and lox71 | 20 |

END OF SEARCH HISTORY

SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2379055 AA 20010125 CA 2000-2379055 20000502
EP 1201759 A1 20020502 EP 2000-922969 20000502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI JP 1999-200997 A 19990714
WO 2000-JP2916 W 20000502
AB Vectors for Cre-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The loxP sequence consisting of a reverse repetitive sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, a mutation is transferred into a part of the reverse repetitive sequence 1 or a part of the reverse repetitive sequence 2. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Mouse, rat, rabbit, guinea pig, pig, sheep, or goat can be used as transgenic animals. Various gene ***trap*** ***vectors*** were constructed and introduced into ES cells. ES cell colonies contg. a single copy of the vector and retaining the ***lox71*** sequence were selected by .beta.-gal marker gene expression. Transgenic mouse were generated.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
DUPLICATE 1
AN 2000:433494 BIOSIS
DN PREV200000433494
TI Exchangeable gene trap using the Cre/mutated lox system.
AU Araki, Kimi; Imaizumi, Takashi; Sekimoto, Tomohisa; Yoshinobu, Kumiko; Yoshimuta, Junichiro; Akizuki, Miwa; Miura, Katsutaka; Araki, Masatake; Yamamura, Ken-ichi [Reprint author]
CS Institute of Molecular Embryology and Genetics, Kumamoto University School of Medicine, Kuhonji 4-24-1, Kumamoto, 862-0976, Japan
SO Cellular and Molecular Biology (Noisy-Le-Grand), (July, 1999) Vol. 45, No. 5, pp. 737-750. print.
DT Article
LA English
ED Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002
AB The gene trap technique is a powerful approach for characterizing and mutating genes involved in mouse development. However, one shortcoming of gene trapping is the relative inability to induce subtle mutations. This problem can be overcome by introducing a knock-in system into the gene trap strategy. Here, we have constructed a new gene ***trap*** ***vector*** , pU-Hachi, employing the Cre-mutated lox system (Araki et al., 1997), in which a pair of mutant lox, ***lox71*** and ***lox66*** , was used to promote targeted integrative reaction by Cre recombinase. The pU-Hachi carries splicing acceptor (SA)- ***lox71*** -internal ribosomal entry site (IRES)-beta-geo-pA-loxP-pA-pUC. By using this vector, we can carry out random insertional mutagenesis as the first step, and then we can replace the beta-geo gene with any gene of interest through Cre-mediated integration. We have isolated 109 trap clones electroporated with pU-Hachi, and analyzed their integration patterns by Southern blotting to select those carrying a singlecopy of the ***trap*** ***vector*** . By use of some of these clones, we have succeeded in exchanging the reporter gene at high efficiency, ranging between 20-80%. This integration system is also quite useful for plasmid rescue to recover flanking genomic sequences, because a plasmid vector sequence can be introduced even when the pUC sequence of the ***trap*** ***vector*** is lost through integration into the genome. Thus, this method, termed exchangeable gene trapping, has many advantages as the trapped clones can be utilized to express genes with any type of mutation.

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:265521 CAPLUS
DN 129:36929
TI Selective disruption of genes transiently induced in differentiating mouse embryonic stem cells by using gene trap mutagenesis and site-specific recombination
AU Thorey, Irmgard S.; Muth, Katrin; Russ, Andreas P.; Otte, Jurgen; Reffelmann, Armin; Von Melchner, Harald
CS Laboratory for Molecular Hematology, Department of Hematology, University of Frankfurt Medical School, Frankfurt Am Main, 60590, Germany
SO Molecular and Cellular Biology (1998), 18(5), 3081-3088
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB A strategy employing gene trap mutagenesis and site-specific recombination (Cre/loxP) has been used to identify genes that are transiently expressed during early mouse development. Embryonic stem cells expressing a reporter plasmid that codes for neomycin phosphotransferase and Escherichia coli LacZ were infected with a retroviral gene ***trap*** ***vector*** (U3Cre) carrying coding sequences for Cre recombinase (Cre) in the U3 region. Activation of Cre expression from integrations into active genes resulted in a permanent switching between the two selectable marker genes and consequently the expression of .beta.-galactosidase (.beta.-Gal). As a result, clones in which U3Cre had disrupted genes that were only transiently expressed could be selected. Moreover, U3Cre-activating cells acquired a cell autonomous marker that could be traced to cells and tissues of the developing embryo. Thus, when two of the clones with inducible U3Cre integrations were passaged in the germ line, they generated spatial patterns of .beta.-Gal expression.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s lox66 or lox71
L1 22 LOX66 OR LOX71

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 19 DUP REM L1 (3 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 19 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:409706 CAPLUS
DN 142:458113
TI Methods for producing a paired tag from a nucleic acid sequence without cloning, and methods of use thereof
IN Smith, Douglas R.; Malek, Joel A.; Mckeman, Kevin J.
PA Agencourt Bioscience Corporation, USA
SO PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2005042781 | A2 | 20050512 | WO 2004-US36141 | 20041029 |
| WO 2005042781 | C1 | 20050811 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-516080P P 20031031
AB Methods for producing a paired tag from a nucleic acid sequence are provided in which the paired tag comprises the 5' end tag and 3' end tag of the nucleic acid sequence. In one embodiment, the nucleic acid sequence comprises two restriction endonuclease recognition sites specific for a restriction endonuclease that cleaves the nucleic acid sequence distally to the restriction endonuclease recognition sites. In another embodiment, the nucleic acid sequence further comprises restriction endonuclease recognition sites specific for a rare cutting restriction endonuclease. In one claim, the method for producing a paired tag from a first nucleic acid fragment, without cloning, comprises (a) joining the 5' and 3' ends of the fragment via a linker such that the linker is located between the 5' end and the 3' end of the first nucleic acid sequence in a circular nucleic acid mol., and (b) cleaving the circular nucleic acid mol., e.g. with a restriction endonuclease that cleaves distal to the restriction endonuclease recognition site in the linker. The paired tag that is produced has a 5' end tag of the first nucleic acid fragment joined to a 3' end tag of the first nucleic acid fragment via the linker. The orientation of the linker(s) and end tags can be reversed. Methods of using paired tags are also provided. In one embodiment, paired tags are used to characterize a nucleic acid sequence. In a particular embodiment, the nucleic acid sequence is a genome. In one embodiment, the characterization of a nucleic acid sequence is karyotyping. Alternatively, in another embodiment, the characterization of a nucleic acid sequence is mapping of the sequence. In a further embodiment, a method is provided for identifying nucleic acid sequences that encode at least two interacting proteins. The invention represents a development for the whole genome approach to genome sequencing because the ability to produce paired end tags from large insert clones increases the no. of large insert clones that can be used. The tags represent long-range scaffolding information that is necessary to avoid misassemblies of genomic regions that have complex repeats, significant levels of allelic polymorphism, or recent segmental duplications.

L2 ANSWER 2 OF 19 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 1
AN 2005220518 EMBASE
TI Characterization of an exchangeable gene trap using pU-17 carrying a stop codon-.beta.geo cassette.
AU Taniwaki T.; Haruna K.; Nakamura H.; Sekimoto T.; Oike Y.; Imaizumi T.; Saito F.; Muta M.; Soejima Y.; Utoh A.; Nakagata N.; Araki M.; Yamamura K.-I.; Araki K.
CS K.-I. Yamamura, Institute of Molecular Embryology and Genetics, Kumamoto University, Kuhonji 4-24-1, Kumamoto 862-0976, Japan. yamamura@gpo.kumamoto-u.ac.jp
SO Development Growth and Differentiation, (2005) Vol. 47, No. 3, pp. 163-172.
Refs: 38
ISSN: 0012-1592 CODEN: DGDFA5
CY Australia
DT Journal; Article
FS 016 Cancer
022 Human Genetics
LA English
SL English
ED Entered STN: 20050602
Last Updated on STN: 20050602
AB We have developed a new exchangeable gene trap vector, pU-17, carrying the
intron- ***lox71*** -splicing acceptor (SA)-.beta.geo-loxP-pA-lox2272-pSP73-lox511. The SA contains three stop codons in-frame with the ATG of .beta.galactosidase/ neomycin-resistance fusion gene (.beta.geo) that can function in promoter trapping. We found that the trap vector was highly selective for integrations in the introns adjacent to the exon containing the start codon. Furthermore, by using the Cre-mutant lox system, we successfully replaced the .beta.geo gene with the enhanced green fluorescent protein (EGFP) gene, established mouse lines with the replaced clones, removed the selection marker gene by mating with Flp-deleter mice, and confirmed that the replaced EGFP gene was expressed in the same pattern as the .beta.geo gene. Thus, using this pU-17 trap vector, we can initially carry out random mutagenesis, and then convert it to a gain-of-function mutation by replacing the .beta.geo gene with any gene of interest to be expressed under the control of the trapped promoter through Cre-mediated recombination.

L2 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1020109 CAPLUS
DN 141:422008
TI Improved methods for identifying interacting proteins by using a plasmid pair in a modified two hybrid system
IN Pruitt, Steven C.; Hastie, Alexander; Mielnicki, Lawrence
PA Health Research Inc., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2004102157 | A2 | 20041125 | WO 2004-US14613 | 20040510 |
| WO 2004102157 | A3 | 20050630 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005164214 A1 20050728 US 2004-842741 20040510
PRAI US 2003-469342P P 20030509
AB The present invention provides a method for identifying a plurality of pairs of interacting proteins and plasmids for use in the method. The invention provides a plasmid pair adapted for use in a modified two hybrid system wherein first plasmid comprises a coding sequence for a DNA binding domain of a transcription activator (the "DBD plasmid") and the second plasmid comprises a coding sequence for a transcription activation domain of a transcription activator (the "AD plasmid"), and each plasmid further comprises a recombinase recognition site. The method comprises the steps of providing cDNAs encoding test polypeptides, inserting the cDNAs into the first and second plasmids, recombining the first and second plasmids to obtain recombined plasmids, isolating and digesting the recombined plasmids, ligating the restriction fragments to a universal adapter to provide a pool of digested fragments flanked by a universal adapter, selecting and amplifying desired sequences, forming concatamers from the amplified sequences, and sequencing the concatamers to det. the nucleotide sequences encoding a plurality of pairs of interacting proteins.

L2 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1036594 CAPLUS
DN 142:18448
TI Conditional knockout vector for gene trapping and gene targeting using an inducible gene silencer for recombinase-mediated inversion
IN Askew, G. Roger; Kanki, Kim L.
PA Wyeth, John, and Brother Ltd., USA
SO U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

PI US 2004241851 A1 20041202 US 2003-448395 20030530
CA 2428972 AA 20041130 CA 2003-2428972 20030530
PRAI US 2003-448395 A 20030530
AB The invention relates to a method for conditionally knocking out and altering gene function for use in gene trapping and gene targeting. Specifically, the genetic sequence is a inducible gene silencer comprising: (a) a splice acceptor sequence; (b) an internal ribosomal entry site (IRES) sequence; (c) a nucleotide sequence coding for a reporter protein; (d) a polyadenylation sequence; and (e) a pair of oppositely oriented recombination site sequences flanking element (a) through (d), which cause single cycle inversions in the presence of a suitable recombinase enzyme. The invention also provides the sequences of gene silencer, element ***lox71*** and ***lox66*** , Simian virus 40 splice acceptor and polyadenylation signal, and human gene GTX element IRES. The invention further relates to targeting of the inducible gene silencer to intron one of the HPRT locus in mouse ES cells.

L2 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:892887 CAPLUS
DN 139:359864
TI Cellular libraries for in vitro mutagenesis, phenotyping, and gene mapping
IN Threadgill, David W.; Lee, Daekee
PA University of North Carolina, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003093426 | A2 | 20031113 | WO 2003-US13625 | 20030502 |
| WO 2003093426 | A3 | 20040318 | | |
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| CA 2484360 | AA | 20031113 | CA 2003-2484360 | 20030502 |
| US 2004033596 | A1 | 20040219 | US 2003-428977 | 20030502 |
| EP 1501927 | A2 | 20050202 | EP 2003-724380 | 20030502 |
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| PRAI US 2002-377864P | P | 20020502 | | |
| WO 2003-US13625 | W | 20030502 | | |

AB The present invention provides cellular libraries useful for in vitro phenotyping and gene mapping, and methods for using the same. In one embodiment of the present invention, a heterozygous cellular library is provided, the heterozygous cellular library comprising a randomly mutagenized population of isolated cells, wherein each of the isolated cells comprises a marked chromosome comprising a dominant pos. selectable marker. In another embodiment of the present invention, a homozygous cellular library is provided, the homozygous cellular library comprising a randomly mutagenized and homozygosed population of isolated cells. The present invention also provides methods for prepg. a homozygous cellular library. A representative embodiment of the method comprises: (a) providing a heterozygous cellular library comprising a plurality of isolated parent cells; (b) inducing site-specific mitotic recombination in the plurality of isolated parent cells; (c) culturing the plurality of isolated parent cells, where by a population of daughter cells is produced; and (d) selecting daughter cells comprising a homozygous genetic modification, where by a homozygous cellular library is prepd. In one embodiment, the heterozygous cellular libraries and homozygous cellular libraries of the present invention each comprise a population of genetically related cells. The present invention further provides a kit for in vitro phenotyping and gene mapping. Gene targeting methods were used to prep. ES cells comprising a pair of allelic recombination cassettes and a distal chromosome marker. The resulting plates of individual mutagenized ES cells comprise a heterozygous cellular library. The replica libraries are alternately used for prepn. of a homozygous cellular library (Example 4), for phenotypic screening (Example 5), and for gene mapping (Example 6). Replica libraries are cryopreserved as described in Example 3.

L2 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:417883 CAPLUS
DN 139:5641
TI Preparation of artificial antibody library with super-repertory
IN Shimizu, Nobuyoshi; Takayanagi, Atsushi; Okui, Michiyo
PA Keio University, Japan
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003044198 | A1 | 20030530 | WO 2002-JP12236 | 20021122 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| EP 1457559 | A1 | 20040915 | EP 2002-803566 | 20021122 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| PRAI JP 2001-358602 | A | 20011122 | | |
| WO 2002-JP12236 | W | 20021122 | | |

AB This invention provides a method of prepn. of artificial antibody lib. An artificial antibody library with a super-repertory (1011 or more) is constructed by: using a cDNA library as a template, amplifying a fragment contg. the CDR1 and CDR2 regions of the VH or VL region of Ig gene and a fragment contg. the CDR3 region each by the PCR method. The primers for amplification of the antibody fragments were disclosed. The library was further prepd. by integrating the VH library and the VL library, which are less contaminated with unexpressing repertory and have high safety, into an non-expression vector; transferring it into a host; and then shuffling the VH region in the VH library with the VL region in the VL library. The library can be used for diagnosis and drug screening.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:377014 CAPLUS
DN 138:363819
TI Methods for mutating genes in cells and animals using retroviral vector insertional mutagenesis
IN Harrington, John Joseph; Jackson, Paul David; Jiang, Li
PA Athersys, Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003040324 | A2 | 20030515 | WO 2002-US35405 | 20021104 |
| WO 2003040324 | A3 | 20031211 | | |
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| US 2003134421 | A1 | 20030717 | US 2002-288555 | 20021104 |
| EP 1451295 | A2 | 20040901 | EP 2002-780573 | 20021104 |
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| PRAI US 2001-330978P | P | 20011102 | | |
| WO 2002-US35405 | W | 20021104 | | |

AB The present invention is in the fields of mol. biol., cell biol., and genetics. The invention is directed generally to mutating genes in cells in vitro and in multi-cellular organisms. The invention encompasses methods for mutating genes in cells using polynucleotides that act as insertional mutagens. Such methods are used to achieve mutation of a single gene to achieve a desired phenotype as well as mutation of multiple genes, required cumulatively to achieve a desired phenotype, in a cell or in a multi-cellular organism. The invention is also directed to methods of identifying one or more mutated genes, made by the methods of the invention, in cells and in multi-cellular organisms, by means of a tagging property provided by the insertional mutagen(s). The insertional mutagen thus allows identification of one or more genes that are mutated by insertion of an insertional mutagen. The invention is also directed to methods for correlating a phenotype with a gene by screening or selecting cells that have been mutated by an insertional mutagen incorporated into one or more genes in a cell and identifying the gene or genes causing the phenotype by means of a tagging property in one or more of the insertional mutagens. The invention is also directed to cells and multi-cellular organisms created by the methods of the invention and uses of the cells and multicellular organisms. The invention is also directed to libraries of cells created by the methods of the invention and uses of the libraries. An exemplary vector pDKO2 designed to trap transcriptionally active genes using the function of the splice acceptor in the vector is described. PDKO2 (3'LTR-lox-S/A-x-IRES-DR-bGHpA-TK-PGK-lox-Y-5'LTR) contains vector backbone from self-inactivating retroviral vector pSIR and genetic elements including S/A:branch site and splice acceptor (from the intron of an immunoglobin gene heavy chain variable region), lox: ***lox71*** / ***lox66*** sequences, cre recombinase recognition sites, x:stop codons in all 3 reading frames, IRES: wild type internal ribosomal entry site from EMCV, DR:drug resistance gene for selection in the presence of neomycin, bGHpA: bovine growth hormone polyA sequence,
TK:

thymidine kinase, PGK: PGK promoter, and .PHI.:retrovirus packaging signal. Theor., when the vector is integrated into a gene, splicing can occur using endogenous splice donor at the end of exons and the splice acceptor provided by the vector. Once this splicing event occurs, a fusion transcript will be made resulting in a truncated protein of the trapped gene. IRES enables the expression of the drug selection marker when an active promoter is trapped, which allows selection of gene trap event. The retrovirus produced from RetroPack PT67 cells is used to infect Jurkat and gene trapping is detected by RT-PCR in genes for DHFR, HPRT, FasR, and Casp8 using their specific primers.

L2 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:904066 CAPLUS
DN 140:88589
TI Unidirectional Cre-mediated genetic inversion in mice using the mutant loxP pair ***lox66*** / ***lox71***
AU Oberdoerffer, Philipp; Otipoby, Kevin L.; Maruyama, Mitsuo; Rajewsky, Klaus
CS The CBR Institute for Biomedical Research, Harvard Medical School, Boston, MA, 02115, USA
SO Nucleic Acids Research (2003), 31(22), e140/1-e140/7
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The Cre/loxP recombination system is a commonly used tool to alter the mouse genome in a conditional manner by deletion or inversion of loxP-flanked DNA segments. While Cre-mediated deletion is essentially unidirectional, inversion is reversible and therefore does not allow the stable alteration of gene function in cells that constitutively express Cre. Site-directed mutagenesis yielded a pair of asym. loxP sites ( ***lox66*** and ***lox71*** ) that display a favorable forward reaction equil. Here, we demonstrate that ***lox66*** / ***lox71*** mediates efficient and predominantly unidirectional inversion of a switch substrate targeted to the mouse genome in combination with either inducible or cell type-specific cre-transgenes in vivo.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:849821 CAPLUS
DN 137:364382
TI Method for generating conditional reporters by gene trapping using Cre recombinase-mediated site-specific recombination
IN Chambon, Pierre; Ghyselinck, Norbert B.; Schnuetgen, Frank
PA Association pour le Developpement de la Recherche en Genetique Moleculaire
(ADEREGEM), Fr.
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002088353 | A2 | 20021107 | WO 2002-IB2493 | 20020419 |
| WO 2002088353 | A3 | 20030320 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003159160 | A1 | 20030821 | US 2001-843150 | 20010427 |
| EP 1383891 | A2 | 20040128 | EP 2002-733179 | 20020419 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004244071 | A1 | 20041202 | US 2004-475962 | 20040413 |
| PRAI US 2001-843150 | A | 20010427 | | |
| WO 2002-IB2493 | W | 20020419 | | |

AB The invention relates to a method for the stable inversion of a DNA fragment upon recombinase-mediated rearrangements using two sets of two incompatible site-specific recombinase targeting sites (SSRTS) in the same order but in reverse orientation flanking said DNA fragment to be inverted. The invention also relates to a method for the stable inversion of said DNA fragment upon rearrangement mediated by a recombinase such as Cre recombinase. The invention also relates to a method for obtaining a transgenic cell of which at least one allele of a DNA sequence of interest is invalidated by a process of conditional deletion and the genome of which comprises a reporter gene inserted at the place of the DNA fragment deleted by said process of conditional deletion. The invention also concerns a method to generate targeting sites to perform site-specific recombination mediated cassette exchange. The corresponding vectors, host cells, and transgenic animals are claimed.

L2 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:814310 CAPLUS
DN 137:321289
TI Expression systems to produce DNA minicircle lacking bacterial vector sequences from parent plasmid for gene therapy
IN Bigger, Brian W.; Tolmachov, Oleg; Coutelle, Charles
PA Imperial College Innovations Limited, UK
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002083889 | A2 | 20021024 | WO 2002-GB1668 | 20020410 |
| WO 2002083889 | A3 | 20031113 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2358263 | AA | 20021010 | CA 2001-2358263 | 20011004 |
| US 2003005478 | A1 | 20030102 | US 2002-118231 | 20020409 |
| PRAI GB 2001-8968 | A | 20010410 | | |
| US 2001-327029P | P | 20011005 | | |

AB The present invention relates to a method for the prodn. of a minicircle from parent plasmid which has a nucleic sequence flanked by recombination sites. The invention relates to creation of bacterial strains expressing cre recombinase under the tight control of the araC regulon, which can be used to produce large quantities of DNA minicircle in vivo. The invention relates to creation of bacterial strains where both Cre-recombinase and PvuII-endonuclease (PvuII) are inducible expressed, allowing generation of minicircle DNA with concomitant complete or partial elimination of the unwanted recombination products in vivo. The invention further relates to construction of minicircle producing plasmids with attP and attB sites for bacteriophage .phi.C31 integrase. This parent plasmid is exposed to an enzyme which causes recombination at the recombination sites, thereby to form a (I) minicircle comprising the nucleic acid sequence and (ii) a miniplasmid comprising the remainder of the parent plasmid. One recombination site is modified at the 5' end such that its reaction with the enzyme is less efficient than the wild type site, and the other recombination site is modified at the 3' end such that its reaction with the enzyme is less efficient than the wild type site, and the other recombination site is modified at the 3' end such that its reaction with the enzyme is less efficient than the wild type site, both modified sites being located in the minicircle after recombination. This favors the formation of minicircle.

L2 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:914707 CAPLUS
DN 138:12018
TI Vectors with mutated loxP sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Yoshimi
PA Japan Science and Technology Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002345477 | A2 | 20021203 | JP 2001-157567 | 20010525 |
| PRAI JP 2001-157567 | | 20010525 | | |

AB Vectors for Cre-mediated gene trap insertional mutagenesis contg. a mutated loxP sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The loxP sequence consisting of a inverted repeat sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, and having mutations in the inverted repeat sequence 1 or a inverted repeat sequence 2, is used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Transgenic mice having disruptions in Tubedown-1 gene were generated from ES cells by introducing gene trap vectors of the invention.

L2 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:961440 CAPLUS
DN 138:34098
TI Application of mutant recognition sequences in the integration of foreign DNA into a target sequence with destruction of the recognition sequence preventing excision
IN Altmann, Markus; Neuhierl, Bernhard; Hammerschmidt, Wolfgang
PA GSF-Forschungszentrum Fuer Umwelt Und Gesundheit G.m.b.H., Germany
SO Ger., 10 pp.
CODEN: GWXXAW
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

PI DE 10140030 C1 20021219 DE 2001-10140030 20010816
EP 1288295 A2 20030305 EP 2002-16913 20020731
EP 1288295 A3 20030312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
US 2003082723 A1 20030501 US 2002-214722 20020807
JP 2003116551 A2 20030422 JP 2002-235346 20020813
PRAI DE 2001-10140030 A 20010816
AB A method of using variants of recombinase recognition sites in the integration of foreign DNA into a host chromosome is described. The method eliminates the recombination site from the integration product and prevents recombinase-mediated excision or inversion of the integrated DNA. Each of the recognition sequence mutants consists of two recognition sequences sepd. by a spacer. Into the recognition sequence mutations are introduced, so that after the recombination through a sequence-specific recombinase a recognition sequence mutant results, which is no longer recognized by the recombinase. Use of variants of the loxP site to direct cre/loxP-mediated integration without subsequent recombination of the integrated DNA is demonstrated.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:666677 CAPLUS
DN 138:50469
TI Cre recombinase-mediated inversion using ***lox66*** and ***lox71*** : method to introduce conditional point mutations into the CREB-binding protein
AU Zhang, Zuwen; Lutz, Beat
CS Research Group Molecular Genetics of Behavior, Max-Planck-Institute of Psychiatry, Munich, D-80804, Germany
SO Nucleic Acids Research (2002), 30(17), e90/1-e90/8
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB CREB-binding protein (CBP) is a multifunctional cofactor implicated in many intracellular signal transduction pathways. We aimed to investigate the involvement of CBP in the cAMP response element-binding protein (CREB)-mediated pathway. The point mutation Tyr658Ala in the CREB-binding domain (CBD) was shown to abolish the binding activity of CBP to phospho-CREB, the activated form of CREB. By using a mutant Cre/loxP recombination system, this point mutation was aimed to be generated in the mouse genome in a tissue- and time-specific manner. A targeting construct in which CBD exon 5 and inverted exon 5* contg. the point mutation flanked by two mutant loxP sites ( ***lox66*** and ***lox71*** ) oriented in a head-to-head position was generated. When Cre recombinase is present, the DNA flanked by the two mutant loxP sites is inverted, forming one loxP and one double mutated loxP site. As the double mutated loxP site shows low affinity for Cre recombinase, the favorable reaction leads to a product where the mutated exon 5* is placed into the position to be correctly transcribed and spliced. Inversion was obsd. to be complete in both bacteria and mouse embryonic stem cells. Our results indicate that this Cre- mediated inversion method is a valuable tool to introduce point mutations in the mouse genome in a regulatable manner.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:833542 CAPLUS
DN 135:367645
TI Vectors with mutated loxP sequence and antisense promoter for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Taniguchi, Masaru; Karasawa, Mika
PA Japan Science and Technology Corporation, Japan
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001085973 A1 20011115 WO 2000-JP5824 20000829
W: AU, CA, US
RW: DE, FR, GB, IT
JP 2001321174 A2 20011120 JP 2000-138938 20000511
CA 2379095 AA 20011115 CA 2000-2379095 20000829
AU 2000067337 A5 20011120 AU 2000-67337 20000829
EP 1281765 A1 20030205 EP 2000-955091 20000829
R: DE, FR, GB, IT
PRAI JP 2000-138938 A 20000511
WO 2000-JP5824 W 20000829
AB Vectors for Cre recombinase-mediated gene trap insertional mutagenesis contg. a mutated loxP sequence, antisense promoter transfer vector, and use in generation of embryonic stem cells (ES cells) having deficient expression of normal wild type genes, or gene knockout animals, are disclosed. The loxP sequence consisting of a inverted repeat sequence, ***lox71*** or ***lox66*** , or FRT sequence, and spacer sequence, are used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, are also used. Reporter genes or selection marker genes such as neomycin resistance gene (neoR), puromycin resistance gene, hygromycin resistance gene, and diphtheria toxin gene, are used for ES cell prepn. Thymidine kinase gene or diphtheria toxin gene fused to phosphoglycero kinase gene promoter can be also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Gene knockout mice are claimed. By inserting a powerful promoter into a definite position in a mutated locus, wherein the insertion of the gene trap vector of the trapped clone has occurred, in the direction opposite to the endogenous gene, moreover, the antisense RNA against the trapped gene is compulsively transcribed and thus the transcription product from the wild type gene is disrupted.

L2 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:300862 CAPLUS
DN 134:321557
TI Conditional gene trapping construct for mutational inactivation of all genes in mammalian cells
IN Kuehn, Ralf; Von Melchener, Harald; Altschmied, Joachim
PA Artemis Pharmaceuticals Gmbh, Germany; Frankgen Biotechnologie Ag
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001029208 A1 20010426 WO 2000-EP10162 20001016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1092768 A1 20010418 EP 1999-120592 19991016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
CA 2387737 AA 20010426 CA 2000-2387737 20001016
EP 1222262 A1 20020717 EP 2000-974397 20001016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
JP 2003512053 T2 20030402 JP 2001-532191 20001016
PRAI EP 1999-120592 A 19991016
US 1999-162016P P 19991027
WO 2000-EP10162 W 20001016
AB The present invention relates to a gene trapping construct which causes conditional mutations in genes, and the use of this gene trapping construct to mutationally inactivate all cellular genes. The gene trapping constructs comprises a functional DNA segments inserted in sense or antisense direction relative to the transcriptional orientation of the gene to be trapped and being flanked by two recombinase recognition sequences RRSs which are specific to site specific recombinase capable of inverting double stranded DNA segment. In addn. the invention relates to a cell, preferably a mammalian cell which contains the above mentioned construct. Moreover, the invention relates to the use of said cell for identification and/or isolation of genes and for the creation of transgenic organisms to study gene function at various developmental stages, including the adult. In conclusion, the present invention provides a process which enables a temporally and/or spatially restricted inactivation of all genes that constitute a living organism.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:64171 CAPLUS
DN 134:126757
TI Vectors with mutated loxP sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Yamamura, Ken-ichi; Araki, Kimi
PA Transgenic Inc., Japan
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001005987 A1 20010125 WO 2000-JP2916 20000502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2379055 AA 20010125 CA 2000-2379055 20000502
EP 1201759 A1 20020502 EP 2000-922969 20000502

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
AU 778719 B2 20041216 AU 2000-43176 20000502
PRAI JP 1999-200997 A 19990714
WO 2000-JP2916 W 20000502
AB Vectors for Cre-mediated gene trap insertional mutagenesis contg. a mutated loxP sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The loxP sequence consisting of a reverse repetitive sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, a mutation is transferred into a part of the reverse repetitive sequence 1 or a part of the reverse repetitive sequence 2. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Mouse, rat, rabbit, guinea pig, pig, sheep, or goat can be used as transgenic animals. Various gene trap vectors were constructed and introduced into ES cells. ES cell colonies contg. a single copy of the vector and retaining the ***lox71*** sequence were selected by .beta.-gal marker gene expression. Transgenic mouse were generated.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:669158 CAPLUS
DN 136:336146
TI Construction and application of mouse HPRT targeting vector with Cre recombinase recognition site ***lox66***
AU Zheng, Jingmin; Li, Jian; Yang, Hua; Fu, Jiliang
CS Department of Medical Genetics, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SO Dier Junyi Daxue Xuebao (2001), 22(6), 538-541
CODEN: DJXUE5; ISSN: 0258-879X
PB Dier Junyi Daxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The vector pSP-HPRT- ***lox66*** -Neo contg. Cre recombinase recognition site ***lox66*** for mouse HPRT gene targeting in embryonic stem (ES) cells was constructed from HPRT genomic DNA fragment and synthetic oligonucleotides by common mol. cloning techniques. ES cells transfected with the linearized pSP-HPRT- ***lox66*** -Neo DNA by electroporation were cultured in G418/6-TG drug selection medium. The recombination efficiency of this vector was tested. The main components of pSP-HPRT- ***lox66*** -Neo were a pos. selection gene Neo, ***lox66*** , long and short homologous fragments of mouse HPRT gene, and plasmid backbone. Twenty inactivated ES cell clones with HPRT gene were obtained. The results showed that an effective replacement vector with Cre recombinase recognition site ***lox66*** was constructed and applied to HPRT gene targeting in ES cells.

L2 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:590614 CAPLUS
DN 136:211452
TI Isolation and subcloning of large fragments from BACs and PACs
AU Kaname, Tadashi; Huxley, Clare
CS Imperial College School of Medicine, London, SW7 2AZ, UK
SO BioTechniques (2001), 31(2), 273,276,278
CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton Publishing Co.
DT Journal
LA English
AB An improvement of the method using a mini-gel system with normal electrophoresis that is widely used in labs. is described. This modified method is simple, quick, and reliable for isolating large fragments from bacterial artificial chromosomes (BACs) and PI-derived artificial chromosomes (PACs). A new BAC vector, designated pBeloBAC66D1, which has a mutant loxP ( ***lox66*** ) and neomycin-resistant gene was constructed. To subclone a 155-kb insert of the human HPRT gene in a BAC into the new vector, 2.2 .mu.g BAC DNA was digested with NotI. The DNA fragments were then sepd. by electrophoresis through an agarose mini-gel and isolated by agarase treatment of the gel. The clones were checked by polymerase chain reaction targeted to the neomycin-resistant gene and to exon 9 of the human HPRT gene and by digestion with restriction enzymes followed by pulsed field gel electrophoresis. Of eight incorrect clones, five had only the self-ligated new vector, one had self-ligated pBeloBAC11, and two probably had no plasmids. The use of this improved protocol allowed a large fragment to be easily and efficiently subcloned into a new vector.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 19 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2
AN 2000:433494 BIOSIS
DN PREV200000433494
TI Exchangeable gene trap using the Cre/mutated lox system.
AU Araki, Kimi; Imaizumi, Takashi; Sekimoto, Tomohisa; Yoshinobu, Kumiko; Yoshimuta, Junichiro; Akizuki, Miwa; Miura, Katsutaka; Araki, Masatake; Yamamura, Ken-ichi [Reprint author]
CS Institute of Molecular Embryology and Genetics, Kumamoto University School of Medicine, Kuhonji 4-24-1, Kumamoto, 862-0976, Japan
SO Cellular and Molecular Biology (Noisy-Le-Grand), (July, 1999) Vol. 45, No. 5, pp. 737-750. print.
DT Article
LA English
ED Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002
AB The gene trap technique is a powerful approach for characterizing and mutating genes involved in mouse development. However, one shortcoming of gene trapping is the relative inability to induce subtle mutations. This problem can be overcome by introducing a knock-in system into the gene trap strategy. Here, we have constructed a new gene trap vector, pU-Hachi, employing the Cre-mutated lox system (Araki et al., 1997), in which a pair of mutant lox, ***lox71*** and ***lox66*** , was used to promote targeted integrative reaction by Cre recombinase. The pU-Hachi carries splicing acceptor (SA)- ***lox71*** -internal ribosomal entry site (IRES)-beta-geo-pA-loxP-pA-pUC. By using this vector, we can carry out random insertional mutagenesis as the first step, and then we can replace the beta-geo gene with any gene of interest through Cre-mediated integration. We have isolated 109 trap clones electroporated with pU-Hachi, and analyzed their integration patterns by Southern blotting to select those carrying a singlecopy of the trap vector. By use of some of these clones, we have succeeded in exchanging the reporter gene at high efficiency, ranging between 20-80%. This integration system is also quite useful for plasmid rescue to recover flanking genomic sequences, because a plasmid vector sequence can be introduced even when the pUC sequence of the trap vector is lost through integration into the genome. Thus, this method, termed exchangeable gene trapping, has many advantages as the trapped clones can be utilized to express genes with any type of mutation.

=> s loxP and muta?
L3 1556 LOXP AND MUTA?

=> s l3 and vector
L4 259 L3 AND VECTOR

=> s l4 and invert repeat
L5 0 L4 AND INVERT REPEAT

=> s l4 and inverted repeat
L6 3 L4 AND INVERTED REPEAT

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 3 DUP REM L6 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:914707 CAPLUS
DN 138:12018
TI Vectors with ***mutated*** ***loxP*** sequence for Cre-mediated gene-trap-based insertional ***mutagenesis*** , and use in transgenic or gene knockout methods
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Yoshimi
PA Japan Science and Technology Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002345477 | A2 | 20021203 | JP 2001-157567 | 20010525 |
| PRAI JP 2001-157567 | | 20010525 | | |

AB Vectors for Cre-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The ***loxP*** sequence consisting of a ***inverted*** ***repeat*** sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, and having ***mutations*** in the ***inverted*** ***repeat*** sequence 1 or a ***inverted*** ***repeat*** sequence 2, is used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the ***vector*** into embryonic stem (ES) cells is claimed. Transgenic mice having disruptions in Tubedown-1 gene were generated from ES cells by introducing gene trap vectors of the invention.

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:833542 CAPLUS
DN 135:367645
TI Vectors with ***mutated*** ***loxP*** sequence and antisense promoter for Cre-mediated gene-trap-based insertional ***mutagenesis*** , and use in transgenic or gene knockout methods
IN Taniguchi, Masaru; Karasawa, Mika
PA Japan Science and Technology Corporation, Japan
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent

LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001085973 | A1 | 20011115 | WO 2000-JP5824 | 20000829 |
| | W: AU, CA, US | | | | |
| | RW: DE, FR, GB, IT | | | | |
| | JP 2001321174 | A2 | 20011120 | JP 2000-138938 | 20000511 |
| | CA 2379095 | AA | 20011115 | CA 2000-2379095 | 20000829 |
| | AU 2000067337 | A5 | 20011120 | AU 2000-67337 | 20000829 |
| | EP 1281765 | A1 | 20030205 | EP 2000-955091 | 20000829 |
| | R: DE, FR, GB, IT | | | | |
| PRAI | JP 2000-138938 | A | 20000511 | | |
| | WO 2000-JP5824 | W | 20000829 | | |

AB Vectors for Cre recombinase-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, antisense promoter transfer ***vector*** , and use in generation of embryonic stem cells (ES cells) having deficient expression of normal wild type genes, or gene knockout animals, are disclosed. The ***loxP*** sequence consisting of a ***inverted*** ***repeat*** sequence, lox71 or lox66, or FRT sequence, and spacer sequence, are used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, are also used. Reporter genes or selection marker genes such as neomycin resistance gene (neoR), puromycin resistance gene, hygromycin resistance gene, and diphtheria toxin gene, are used for ES cell prepn. Thymidine kinase gene or diphtheria toxin gene fused to phosphoglycero kinase gene promoter can be also used. A gene trap method comprising introducing the ***vector*** into embryonic stem (ES) cells is claimed. Gene knockout mice are claimed. By inserting a powerful promoter into a definite position in a ***mutated*** locus, wherein the insertion of the gene trap ***vector*** of the trapped clone has occurred, in the direction opposite to the endogenous gene, moreover, the antisense RNA against the trapped gene is compulsively transcribed and thus the transcription product from the wild type gene is disrupted.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:15859 CAPLUS
DN 128:85136
TI Construction of adenoviral gene vectors for mammalian cells
IN Perricaudet, Michel; Yeh, Patrice; Leblois-Prehaud, Helene
PA Rhone-Poulenc Rorer S.A., Fr.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9747757 | A1 | 19971218 | WO 1997-FR914 | 19970523 |
| | W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | FR 2749857 | A1 | 19971219 | FR 1996-7273 | 19960612 |
| | FR 2749857 | B1 | 19980814 | | |
| | CA 2257916 | AA | 19971218 | CA 1997-2257916 | 19970523 |
| | AU 9730377 | A1 | 19980107 | AU 1997-30377 | 19970523 |
| | AU 726442 | B2 | 20001109 | | |
| | EP 906443 | A1 | 19990407 | EP 1997-925133 | 19970523 |
| | EP 906443 | B1 | 20050810 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI | | | | |
| | BR 9709700 | A | 19990810 | BR 1997-9700 | 19970523 |
| | JP 2000511779 | T2 | 20000912 | JP 1998-501269 | 19970523 |
| | ZA 9705134 | A | 19971231 | ZA 1997-5134 | 19970610 |
| | US 6630322 | B1 | 20031007 | US 1998-194960 | 19981207 |
| | NO 9805739 | A | 19981208 | NO 1998-5739 | 19981208 |
| | KR 2000016524 | A | 20000325 | KR 1998-710112 | 19981210 |
| PRAI | FR 1996-7273 | A | 19960612 | | |
| | WO 1997-FR914 | W | 19970523 | | |

AB The invention discloses circular and replicating DNA mols., useful in gene therapy, as well as a particularly efficient method for generating them in situ from a ***mutant*** adenovirus-derived ***vector*** . The adenovirus carries a deletion ***mutation*** in the E1 gene. The DNA sequences carried by the adenoviral vectors are a gene of interest, replication origins from viruses such as the Epstein-Barr virus (EBV) and papillomavirus, ARS sequences, and an inducible promoter controlling the Cre recombinase gene. The promoter is derived from mouse mammary tumor virus and is inducible by dexamethason or tetracycline. The viral replication origin regions are dependent on site-specific recombination. The viral vectors also contain ***inverted*** ***repeat*** sequences from the P1 phage ***loxP*** region which are responsive to Cre recombinase. The method is exemplified by constructing a viral ***vector*** contg. the EBV EBNA1 gene and oriP region, a mammalian cell-functional gene promoter, and the IRES genetic element from encephalomyocarditis virus.

=> s loxP

L8 4123 LOXP

=> s l8 and (trap? (3a) vector)
L9 34 L8 AND (TRAP? (3A) VECTOR)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 20 DUP REM L9 (14 DUPLICATES REMOVED)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 20 DUP REM L10 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 20 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2005220518 EMBASE
TI Characterization of an exchangeable gene trap using pU-17 carrying a stop codon-.beta.geo cassette.
AU Taniwaki T.; Haruna K.; Nakamura H.; Sekimoto T.; Oike Y.; Imaizumi T.; Saito F.; Muta M.; Soejima Y.; Utoh A.; Nakagata N.; Araki M.; Yamamura K.-I.; Araki K.
CS K.-I. Yamamura, Institute of Molecular Embryology and Genetics, Kumamoto University, Kuhonji 4-24-1, Kumamoto 862-0976, Japan. yamamura@gpo.kumamoto-u.ac.jp
SO Development Growth and Differentiation, (2005) Vol. 47, No. 3, pp. 163-172.
Refs: 38
ISSN: 0012-1592 CODEN: DGDFA5
CY Australia
DT Journal; Article
FS 016 Cancer
022 Human Genetics
LA English
SL English
ED Entered STN: 20050602
Last Updated on STN: 20050602
AB We have developed a new exchangeable gene ***trap*** ***vector*** , pU-17, carrying the intron-lox71-splicing acceptor (SA)-.beta.geo-***loxP*** -pA-lox2272-pSP73-lox511. The SA contains three stop codons in-frame with the ATG of .beta.galactosidase/ neomycin-resistance fusion gene (.beta.geo) that can function in promoter trapping. We found that the ***trap*** ***vector*** was highly selective for integrations in the introns adjacent to the exon containing the start codon. Furthermore, by using the Cre-mutant lox system, we successfully replaced the .beta.geo gene with the enhanced green fluorescent protein (EGFP) gene, established mouse lines with the replaced clones, removed the selection marker gene by mating with Flp-deleter mice, and confirmed that the replaced EGFP gene was expressed in the same pattern as the .beta.geo gene. Thus, using this pU-17 ***trap*** ***vector*** , we can initially carry out random mutagenesis, and then convert it to a gain-of-function mutation by replacing the .beta.geo gene with any gene of interest to be expressed under the control of the trapped promoter through Cre-mediated recombination.

L11 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:780852 CAPLUS
DN 141:272597
TI Gene trap system for transiently expressed genes using Cre/ ***loxP*** ***trap*** ***vector*** and reporter ***vector***
IN Suzuki, Noboru
PA Japan Science and Technology Agency, Japan
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004081218 | A1 | 20040923 | WO 2004-JP2569 | 20040302 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | JP 2004275037 | A2 | 20041007 | JP 2003-68307 | 20030313 |
| PRAI | JP 2003-68307 | A | 20030313 | | |

AB It is intended to provide a gene trap system by which any genes including a transiently expressed gene can be trapped. A gene is trapped by a gene ***trap*** ***vector*** using Cre recombinase gene from bacteriophage P1 and the expression of the thus trapped gene is converted into constitutional expression of another reporter gene. The reporter vector carries a promoter functional in the cell, 1st ***loxP*** sequence, drug resistance gene, transcriptional termination sequence, 2nd

***loxP*** sequence, and a reporter gene. The gene ***trap*** ***vector*** carries a splicing acceptor site, internal ribosomal entry site (IRES), nuclear localization signal-added Cre recombinase gene, 1st splicing donor site, structural gene promoter, drug resistance gene, 2nd splicing donor site. The method involves transforming cells with the reporter vector, further transforming cells with the ***trap*** ***vector*** , selecting the cells lacking reporter activity, placing selected cells under defined condition, and selecting cells showing reporter activity. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Non-human transgenic animal transformed with the vectors are claimed.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1036594 CAPLUS
DN 142:18448
TI Conditional knockout ***vector*** for gene ***trapping*** and gene targeting using an inducible gene silencer for recombinase-mediated inversion
IN Askew, G. Roger; Kanki, Kim L.
PA Wyeth, John, and Brother Ltd., USA
SO U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004241851 | A1 | 20041202 | US 2003-448395 | 20030530 |
| CA 2428972 | AA | 20041130 | CA 2003-2428972 | 20030530 |

PRAI US 2003-448395 A 20030530
AB The invention relates to a method for conditionally knocking out and altering gene function for use in gene trapping and gene targeting. Specifically, the genetic sequence is a inducible gene silencer comprising: (a) a splice acceptor sequence; (b) an internal ribosomal entry site (IRES) sequence; (c) a nucleotide sequence coding for a reporter protein; (d) a polyadenylation sequence; and (e) a pair of oppositely oriented recombination site sequences flanking element (a) through (d), which cause single cycle inversions in the presence of a suitable recombinase enzyme. The invention also provides the sequences of gene silencer, element lox71 and lox66, Simian virus 40 splice acceptor and polyadenylation signal, and human gene GTX element IRES. The invention further relates to targeting of the inducible gene silencer to intron one of the HPRT locus in mouse ES cells.

L11 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:5518 CAPLUS
DN 138:50824
TI Gene-trap identification of host cell proteins required for hepatitis C virus replication
IN Kolykhalov, Alexander Alexandrovich
PA USA
SO U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2003004329 | A1 | 20030102 | US 2002-104398 | 20020322 |

PRAI US 2001-278157P P 20010323
AB The present invention relates to the field of antivirus therapy, esp. the treatment or prevention of hepatitis C virus (HCV). Provided are methods that facilitate the identification of host cell genes required for the replication of HCV. More specifically the methods allow to identify host cell proteins. Also provided are methods of identifying compds. that inhibit the activity(ies) of products of these genes required for HCV replication in host cells, and that therefore inhibit HCV replication. These compds. are useful as HCV antiviral pharmaceutical agents to treat or prevent HCV infections in humans. Also provided are novel host cell genes identified by these methods; HCV replicons comprising both a pos. and a neg. selectable marker gene; and cell lines comprising said replicons.

L11 ANSWER 5 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2003441651 EMBASE
TI Overlapping but Distinct Profiles of Gene Expression Elicited by Glucocorticoids and Progestins.
AU Wan Y.; Nordeen S.K.
CS Y. Wan, Dept. of Pathol./Prog. Molec. Biol., Univ. of Colorado Hlth. Sci. Center, Denver, CO 80262, United States. steve.nordeen@uchsc.edu
SO Recent Progress in Hormone Research, (2003) Vol. 58, pp. 199-226.
Refs: 70
ISSN: 0079-9963 CODEN: RPHRA6
CY United States
DT Journal; General Review
FS 003 Endocrinology
022 Human Genetics
LA English
SL English
ED Entered STN: 20031201
Last Updated on STN: 20031201
AB Glucocorticoids and progestins bind to receptors that share many structural and functional similarities, including virtually identical DNA recognition specificity. Nonetheless, the two hormones mediate very distinct biological functions. For example, progestins are associated with the incidence and progression of breast cancer, whereas glucocorticoids are growth suppressive in mammary cancer cells. To understand the mechanisms that engender biological specificity, we have employed two systematic approaches to identify genes that are differentially regulated by the two hormones. The first strategy is to utilize Affymetrix oligonucleotide arrays to compare glucocorticoid- and progestin-regulated gene expression in a human breast cancer cell line. This global analysis reveals that the two hormones regulate overlapping but distinct sets of genes, including 31 genes that are differentially regulated. Surprisingly, the set of differentially regulated genes was almost as large as the set of genes regulated by both hormones. Examination of the set of differentially regulated genes suggests mechanisms behind the distinct growth effects of the two hormones in breast cancer. The differential regulation of four genes representing different regulatory patterns was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot analyses. Treatment with cycloheximide or mifepristone (RU486) indicates that the regulation is a primary, receptor-mediated event. The second strategy is to employ a retroviral promoter trap and Cre/ ***loxP*** -mediated, site-specific recombination to identify genes that are differentially regulated by glucocorticoids and progestins. A mouse fibroblast cell line (4F) stably expressing both glucocorticoid receptor (GR) and progesterone receptor (PR) and containing a single copy of a multifunctional selection plasmid was generated. This line was transduced with a self-inactivating retroviral promoter ***trap*** ***vector*** carrying coding sequences for Cre-recombinase (Cre) in the U3 region. Integration of the provirus places Cre expression under the control of genomic flanking sequence. Activation of Cre expression from integration into active genes results in a permanent switch between the selectable marker genes that convert the cells from neomycin resistant to hygromycin resistant. Selection for hygromycin resistance after hormone treatment yields recombinants in which Cre sequences in the U3 region are expressed from hormone-inducible, upstream cellular promoters. Because Cre-mediated recombination is a permanent event, the expression of the selectable marker genes is independent of ongoing Cre expression. Thus, this system permits the identification of genes that are transiently or weakly induced by hormone. Detailed analyses of genes identified in these studies will furnish a mechanistic understanding of differential regulation by glucocorticoids and progestins.

L11 ANSWER 6 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2003190452 EMBASE
TI Investigation of the transcription in C6 cells trapped by a novel gene ***trap*** ***vector*** of the convergent type.
AU Kutsuwada C.; Miyashita A.; Sasaki T.; Odani S.; Kuwano R.
CS C. Kutsuwada, Department of Molecular Genetics, Brain Research Institute, Niigata University, 1-757 Asahimachi-dori, Niigata 951-8510, Japan
SO Acta Medica et Biologica, (2003) Vol. 51, No. 1, pp. 1-11.
Refs: 26
ISSN: 0567-7734 CODEN: AMBNAS
CY Japan
DT Journal; Article
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20030522
Last Updated on STN: 20030522
AB The interference of transcription by antisense transcripts is now regarded as one of the regulatory mechanisms of gene expression. The overlapping of genes in opposite strands has recently attracted much attention because of their potential association with human diseases. The regulatory mechanism of the overlapping gene itself is also of considerable interest from the view point of gene expression. We designed a novel gene ***trap*** ***vector*** (GTV) that can be transcribed bidirectionally. It contained promoters, dual and orientation-specific reporter genes (.beta.-galactosidase and green fluorescent protein), drug-resistant genes, and SV40 polyadenylation signal flanked by ***loxP*** sites. C6 cell lines stably integrated with the GTV were established by selection with antibiotics. Expression patterns of sense and antisense strands around the ***trap*** ***vector*** examined by the two reporter genes and their transcripts varied substantially by cell lines: some of this was attributable to interference by antisense transcription, but a portion seemed to be under the control of unknown mechanisms. These results proved the present GTV to be useful as a model system for the study of bidirectional transcription in gene expression.

L11 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:970816 CAPLUS
DN 138:50870
TI Construction of ***trapping*** ***vector*** for preparation transgenic mouse with gene knocked out
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Kimi
PA Japan Science and Technology Corporation, Japan

SO Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002369689 | A2 | 20021224 | JP 2001-157568 | 20010525 |
| PRAI JP 2001-157568 | | 20010525 | | |

AB The invention provides a process of construction of ***trapping*** ***vector*** for prepn. transgenic mouse with gene knocked out. The ***trapping*** ***vector*** consists of several patterns of combination of inverted repeating sequence, spacer, wild type and mutate ***loxP*** sequence. The invention also provides a DNA and encoding protein sequence of gene Ayu6003 ***trapped*** with by ***trapping*** ***vector*** which is sequence homolog of E. coli Ftsj gene. The invention also provided a transgenic mouse with Ayu6003 disrupted which can be used for drug screening.

L11 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:914707 CAPLUS
DN 138:12018
TI Vectors with mutated ***loxP*** sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Yoshimi
PA Japan Science and Technology Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002345477 | A2 | 20021203 | JP 2001-157567 | 20010525 |
| PRAI JP 2001-157567 | | 20010525 | | |

AB Vectors for Cre-mediated gene trap insertional mutagenesis contg. a mutated ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The ***loxP*** sequence consisting of a inverted repeat sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, and having mutations in the inverted repeat sequence 1 or a inverted repeat sequence 2, is used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Transgenic mice having disruptions in Tubedown-1 gene were generated from ES cells by introducing gene trap vectors of the invention.

L11 ANSWER 9 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2002220355 EMBASE
TI Identification of genes differentially regulated by glucocorticoids and progestins using a Cre/loxP-mediated retroviral promoter-trapping strategy.
AU Wan Y.; Nordeen S.K.
CS S.K. Nordeen, Department of Pathology B216, Univ. Colorado Health Sci. Center, 4200 East 9th Avenue, Denver, CO 80262, United States. steve.nordeen@uchsc.edu
SO Journal of Molecular Endocrinology, (2002) Vol. 28, No. 3, pp. 177-192. Refs: 51
ISSN: 0952-5041 CODEN: JMLEEI
CY United Kingdom
DT Journal; Article
FS 003 Endocrinology
022 Human Genetics
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20020711
Last Updated on STN: 20020711
AB Glucocorticoids and progestins are two classes of steroid hormone with very distinct biological functions. However, the glucocorticoid receptor (GR) and the progesterone receptor (PR) share many structural and functional similarities. One way that glucocorticoids and progestins can exert different biological effects is through their different abilities to regulate the expression of certain target genes. A strategy employing a retroviral promoter-trap and Cre/ ***loxP*** -mediated site-specific recombination has been developed to identify genes that are differentially regulated by glucocorticoids and progestins. A mouse fibroblast cell line (4F) stably expressing both GR and PR and containing a single copy of a multifunctional selection plasmid is generated. This line is transduced with a self-inactivating retroviral promoter- ***trap*** ***vector*** carrying coding sequences for Cre-recombinase (Cre) in the U3 region. Integration of the provirus places Cre expression under the control of a genomic flanking sequence. Activation of Cre expression from integration into active genes results in a permanent switch between the selectable marker genes that converts the cells from neomycin-resistant to hygromycin-resistant. Selection for hygromycin resistance after hormone treatment yields recombinants in which Cre sequences in the U3 region are expressed from hormone-inducible upstream cellular promoters. Because Cre-mediated recombination is a permanent event, the expression of the selectable marker genes is independent of ongoing Cre expression. Thus this system permits the identification of genes that are transiently or weakly induced by hormone.

L11 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:833542 CAPLUS
DN 135:367645
TI Vectors with mutated ***loxP*** sequence and antisense promoter for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Taniguchi, Masaru; Karasawa, Mika
PA Japan Science and Technology Corporation, Japan
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001085973 | A1 | 20011115 | WO 2000-JP5824 | 20000829 |
| W: AU, CA, US | | | | |
| RW: DE, FR, GB, IT | | | | |
| JP 2001321174 | A2 | 20011120 | JP 2000-138938 | 20000511 |
| CA 2379095 | AA | 20011115 | CA 2000-2379095 | 20000829 |
| AU 2000067337 | A5 | 20011120 | AU 2000-67337 | 20000829 |
| EP 1281765 | A1 | 20030205 | EP 2000-955091 | 20000829 |
| R: DE, FR, GB, IT | | | | |
| PRAI JP 2000-138938 | A | 20000511 | | |
| WO 2000-JP5824 | W | 20000829 | | |

AB Vectors for Cre recombinase-mediated gene trap insertional mutagenesis contg. a mutated ***loxP*** sequence, antisense promoter transfer vector, and use in generation of embryonic stem cells (ES cells) having deficient expression of normal wild type genes, or gene knockout animals, are disclosed. The ***loxP*** sequence consisting of a inverted repeat sequence, lox71 or lox66, or FRT sequence, and spacer sequence, are used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, are also used. Reporter genes or selection marker genes such as neomycin resistance gene (neoR), puromycin resistance gene, hygromycin resistance gene, and diphtheria toxin gene, are used for ES cell prepn. Thymidine kinase gene or diphtheria toxin gene fused to phosphoglycero kinase gene promoter can be also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Gene knockout mice are claimed. By inserting a powerful promoter into a definite position in a mutated locus, wherein the insertion of the gene ***trap*** ***vector*** of the ***trapped*** clone has occurred, in the direction opposite to the endogenous gene, moreover, the antisense RNA against the trapped gene is compulsively transcribed and thus the transcription product from the wild type gene is disrupted.

L11 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:300862 CAPLUS
DN 134:321557
TI Conditional gene trapping construct for mutational inactivation of all genes in mammalian cells
IN Kuehn, Ralf; Von Melchener, Harald; Altschmied, Joachim
PA Artemis Pharmaceuticals Gmbh, Germany; Frankgen Biotechnologie Ag
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001029208 | A1 | 20010426 | WO 2000-EP10162 | 20001016 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1092768 | A1 | 20010418 | EP 1999-120592 | 19991016 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CA 2387737 | AA | 20010426 | CA 2000-2387737 | 20001016 |
| EP 1222262 | A1 | 20020717 | EP 2000-974397 | 20001016 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003512053 | T2 | 20030402 | JP 2001-532191 | 20001016 |
| PRAI EP 1999-120592 | A | 19991016 | | |
| US 1999-162016P | P | 19991027 | | |
| WO 2000-EP10162 | W | 20001016 | | |

AB The present invention relates to a gene trapping construct which causes conditional mutations in genes, and the use of this gene trapping construct to mutationally inactivate all cellular genes. The gene trapping constructs comprises a functional DNA segments inserted in sense or antisense direction relative to the transcriptional orientation of the gene to be trapped and being flanked by two recombinase recognition sequences RRSs which are specific to site specific recombinase capable of inverting double stranded DNA segment. In addn. the invention relates to

a cell, preferably a mammalian cell which contains the above mentioned construct. Moreover, the invention relates to the use of said cell for identification and/or isolation of genes and for the creation of transgenic organisms to study gene function at various developmental stages, including the adult. In conclusion, the present invention provides a process which enables a temporally and/or spatially restricted inactivation of all genes that constitute a living organism.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:64171 CAPLUS
DN 134:126757
TI Vectors with mutated ***loxP*** sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Yamamura, Ken-ichi; Araki, Kimi
PA Transgenic Inc., Japan
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001005987 | A1 | 20010125 | WO 2000-JP2916 | 20000502 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2379055 | AA | 20010125 | CA 2000-2379055 | 20000502 |
| EP 1201759 | A1 | 20020502 | EP 2000-922969 | 20000502 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| AU 778719 | B2 | 20041216 | AU 2000-43176 | 20000502 |
| PRAI JP 1999-200997 | A | 19990714 | | |
| WO 2000-JP2916 | W | 20000502 | | |

AB Vectors for Cre-mediated gene trap insertional mutagenesis contg. a mutated ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The ***loxP*** sequence consisting of a reverse repetitive sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, a mutation is transferred into a part of the reverse repetitive sequence 1 or a part of the reverse repetitive sequence 2. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the vector into embryonic stem (ES) cells is claimed. Mouse, rat, rabbit, guinea pig, pig, sheep, or goat can be used as transgenic animals. Various gene trap vectors were constructed and introduced into ES cells. ES cell colonies contg. a single copy of the vector and retaining the lox71 sequence were selected by .beta.-gal marker gene expression. Transgenic mouse were generated.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:279488 CAPLUS
DN 134:306107
TI A conditional gene trapping construct using an antisense sequence flanked by recombinase recognition sites for the disruption of genes
IN Kuhn, Ralf; Von Melchner, Harald
PA Artemis Pharmaceuticals Gmbh, Germany; Frankgen Biotechnologie Ag
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 1092768 | A1 | 20010418 | EP 1999-120592 | 19991016 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CA 2387737 | AA | 20010426 | CA 2000-2387737 | 20001016 |
| WO 2001029208 | A1 | 20010426 | WO 2000-EP10162 | 20001016 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1222262 | A1 | 20020717 | EP 2000-974397 | 20001016 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003512053 | T2 | 20030402 | JP 2001-532191 | 20001016 |
| PRAI EP 1999-120592 | A | 19991016 | | |
| US 1999-162016P | P | 19991027 | | |
| WO 2000-EP10162 | W | 20001016 | | |

AB The present invention relates to a gene trapping construct which causes conditional mutations in genes, and the use of this gene trapping construct to mutationally inactivate all cellular genes. In addn. the invention relates to a cell, preferably a mammalian cell which contains the above mentioned construct. Moreover, the invention relates to the use of said cell for identification and/or isolation of genes and for the creation of transgenic organisms to study gene function at various developmental stages, including the adult. In conclusion, the present invention provides a process which enables a temporally and/or spatially restricted inactivation of all genes that constitute a living organism.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2001099876 EMBASE
TI An efficient system for conditional gene expression in embryonic stem cells and in their in vitro and in vivo differentiated derivatives.
AU Vallier L.; Mancip J.; Markossian S.; Lukaszewicz A.; Dehay C.; Metzger D.; Chambon P.; Samarut J.; Savatier P.
CS P. Savatier, Lab. de Biol. Moleculaire/Cellulaire, Ctr. Natl. de la Rech. Scientifique, Inst. Natl. Rech. Agronomique LA913, 46 Allee d'Italie, 69364 Lyon Cedex 07, France. Pierre.Savatier@ens-lyon.fr
SO Proceedings of the National Academy of Sciences of the United States of America, (27 Feb 2001) Vol. 98, No. 5, pp. 2467-2472.
Refs: 32
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 004 Microbiology
021 Developmental Biology and Teratology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20010412
Last Updated on STN: 20010412
AB We have developed a universally applicable system for conditional gene expression in embryonic stem (ES) cells that relies on tamoxifen-dependent Cre recombinase- ***loxP*** site-mediated recombination and bicistronic gene-trap expression vectors that allow transgene expression from endogenous cellular promoters. Two vectors were introduced into the genome of recipient ES cells, successively: (i) a bicistronic gene- ***trap*** ***vector*** encoding the .beta.-galactosidase/neo(R) fusion protein and the Cre-ER(T2) (Cre recombinase fused to a mutated ligand-binding domain of the human estrogen receptor) and (ii) a bicistronic gene- ***trap*** ***vector*** encoding the hygro(R) protein and the human alkaline phosphatase (hAP), the expression of which is prevented by tandemly repeated stop-of-transcription sequences flanked by loxP sites. In selected clones, hAP expression was shown to be regulated accurately by 4'hydroxy-tamoxifen. Strict hormone-dependent expression of hAP was achieved (i) in vitro in undifferentiated ES cells and embryoid bodies, (ii) in vivo in virtually all the tissues of the 10-day-old chimeric fetus (after injection of 4'hydroxy-tamoxifen to foster mothers), and (iii) ex vivo in primary embryonic fibroblasts isolated from chimeric fetuses. Therefore, this approach can be applied to drive conditional expression of virtually any transgene in a large variety of cell types, both in vitro and in vivo.

L11 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:370758 CAPLUS
DN 134:126625
TI Gene-trap-based target site for Cre-mediated transgenic insertion
AU Hardouin, Nathalie; Nagy, Andras
CS NSERM, Universite Paris, Paris, Fr.
SO Genesis (New York) (2000), 26(4), 245-252
CODEN: GNESFY; ISSN: 1526-954X
PB Wiley-Liss, Inc.
DT Journal
LA English
AB There is an increasing need for tissue-specific gene expression regulatory elements to study normal and disease development in the mouse. However, the cloning and characterization of these elements are time-consuming and costly. Thus, there is a particular need to be able to identify gene expression patterns without having to clone the promoter elements. Gene-trap strategies identify expression patterns assigned for endogenous genes using reporters, such as LacZ or green fluorescent protein (GFP). The gene- ***trap*** ***vector*** randomly inserts into the genome and "steals" regulatory elements for the reporter. Here we describe an improved gene-trap strategy, which allows an efficient Cre recombinase-mediated insertion of any transgene into the trapped loci as a post-integrational modification and links the expression of the transgene to that of the reporter.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:317220 CAPLUS
DN 130:307545
TI Vectors for exon trapping using recombinase systems for in vivo reversal of orientations
PA Natt, Ernst, Germany
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI DE 19747972 | A1 | 19990512 | DE 1997-19747972 | 19971030 |
| PRAI DE 1997-19747972 | | 19971030 | | |

AB Methods of exon trapping in large (100 kb) DNA fragments using vectors that include a recombination system such as cre/ ***loxP*** for in vivo inversion of the cloned sequence are described. The vectors use a BclI cloning site to clone Sau3A partial digest fragments, or an EagI site to clone NotI fragments. The use of the recombination system allows the rapid subcloning of fragments in both orientations in the same vector as well as speeding restriction mapping and exon trapping studies. Vectors for animal cells can be used to assess the effects of antisense transcription on gene expression. These features can be incorporated into bacteriophage, cosmid, BAC, P1, or PAC vectors.

L11 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2000:433494 BIOSIS
DN PREV200000433494
TI Exchangeable gene trap using the Cre/mutated lox system.
AU Araki, Kimi; Imaizumi, Takashi; Sekimoto, Tomohisa; Yoshinobu, Kumiko; Yoshimuta, Junichiro; Akizuki, Miwa; Miura, Katsutaka; Araki, Masatake; Yamamura, Ken-ichi [Reprint author]
CS Institute of Molecular Embryology and Genetics, Kumamoto University School of Medicine, Kuhonji 4-24-1, Kumamoto, 862-0976, Japan
SO Cellular and Molecular Biology (Noisy-Le-Grand), (July, 1999) Vol. 45, No. 5, pp. 737-750. print.
DT Article
LA English
ED Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002
AB The gene trap technique is a powerful approach for characterizing and mutating genes involved in mouse development. However, one shortcoming of gene trapping is the relative inability to induce subtle mutations. This problem can be overcome by introducing a knock-in system into the gene trap strategy. Here, we have constructed a new gene ***trap*** ***vector*** , pU-Hachi, employing the Cre-mutated lox system (Araki et al., 1997), in which a pair of mutant lox, lox71 and lox66, was used to promote targeted integrative reaction by Cre recombinase. The pU-Hachi carries splicing acceptor (SA)-lox71-internal ribosomal entry site (IRES)-beta-geo-pA- ***loxP*** -pA-pUC. By using this vector, we can carry out random insertional mutagenesis as the first step, and then we can replace the beta-geo gene with any gene of interest through Cre-mediated integration. We have isolated 109 trap clones electroporated with pU-Hachi, and analyzed their integration patterns by Southern blotting to select those carrying a singlecopy of the ***trap*** ***vector*** . By use of some of these clones, we have succeeded in exchanging the reporter gene at high efficiency, ranging between 20-80%. This integration system is also quite useful for plasmid rescue to recover flanking genomic sequences, because a plasmid vector sequence can be introduced even when the pUC sequence of the ***trap*** ***vector*** is lost through integration into the genome. Thus, this method, termed exchangeable gene trapping, has many advantages as the trapped clones can be utilized to express genes with any type of mutation.

L11 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:197627 CAPLUS
DN 128:253803
TI Retrovirus-based expression vectors for use in the study of gene expression in mammalian cells
IN Beach, David H.; Hannon, Gregory J.; Conklin, Douglas S.; Sun, Peiquing
PA Cold Spring Harbor Laboratory, USA; Beach, David H.; Hannon, Gregory J.; Conklin, Douglas S.; Sun, Peiquing
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9812339 | A2 | 19980326 | WO 1997-US17579 | 19970922 |
| WO 9812339 | A3 | 19980903 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6025192 | A | 20000215 | US 1996-716926 | 19960920 |
| US 6255071 | B1 | 20010703 | US 1997-820931 | 19970319 |
| AU 9746590 | A1 | 19980414 | AU 1997-46590 | 19970922 |
| AU 738156 | B2 | 20010913 | | |
| EP 932695 | A2 | 19990804 | EP 1997-945369 | 19970922 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002514054 | T2 | 20020514 | JP 1998-515028 | 19970922 |
| AU 773277 | B2 | 20040520 | AU 2001-97181 | 20011211 |
| PRAI US 1996-716926 | A | 19960920 | | |
| US 1997-820931 | A | 19970319 | | |
| AU 1997-46590 | A3 | 19970922 | | |
| WO 1997-US17579 | W | 19970922 | | |

AB Expression vectors for animal cells that use regulatory elements of retroviruses to drive expression of cloned genes are described. These vectors are replication-defective and can be used in improved mammalian complementation screening, functional inactivation of specific essential or non-essential mammalian genes, and identification of mammalian genes modulated by specific stimuli. Construction of plasmids for the manuf. of a no. of such vectors is described.

L11 ANSWER 19 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 1998134409 EMBASE
TI Selective disruption of genes transiently induced in differentiating mouse embryonic stem cells by using gene trap mutagenesis and site-specific recombination.
AU Thorey I.S.; Muth K.; Russ A.P.; Otte J.; Reffelmann A.; Von Melchner H.
CS H. Von Melchner, Laboratory for Molecular Hematology, Department of Hematology, Univ. of Frankfurt Medical School, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany. melchner@em.uni-frankfurt.de
SO Molecular and Cellular Biology, (1998) Vol. 18, No. 5, pp. 3081-3088.
Refs: 39
ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 19980520
Last Updated on STN: 19980520
AB A strategy employing gene trap mutagenesis and site-specific recombination (Cre/ ***loxP*** ) has been used to identify genes that are transiently expressed during early mouse development. Embryonic stem cells expressing a reporter plasmid that codes for neomycin phosphotransferase and Escherichia coli LacZ were infected with a retroviral gene ***trap*** ***vector*** (U3Cre) carrying coding sequences for Cre recombinase (Cre) in the U3 region. Activation of Cre expression from integrations into active genes resulted in a permanent switching between the two selectable marker genes and consequently the expression of .beta.-galactosidase (.beta.-Gal). As a result, clones in which U3Cre had disrupted genes that were only transiently expressed could be selected. Moreover, U3Cre-activating cells acquired a cell autonomous marker that could be traced to cells and tissues of the developing embryo. Thus, when two of the clones with inducible U3Cre integrations were passaged in the germ line, they generated spatial patterns of .beta.-Gal expression.

L11 ANSWER 20 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 97009134 EMBASE
DN 1997009134
TI Identification of genes induced by factor deprivation in hematopoietic cells undergoing apoptosis using gene-trap mutagenesis and site-specific recombination.
AU Russ A.P.; Friedel C.; Ballas K.; Kalina U.; Zahn D.; Strebhardt K.; Von Melchner H.
CS H. Von Melchner, Laboratory for Molecular Hematology, Department of Hematology, Univ. of Frankfurt Medical School, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany. melchner@em.uni-frankfurt.de
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) Vol. 93, No. 26, pp. 15279-15284.
Refs: 38
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 970212
Last Updated on STN: 970212
AB A strategy employing gene-trap mutagenesis and site-specific recombination (Cre/ ***loxP*** ) has been developed to isolate genes that are transcriptionally activated during programmed cell death. Interleukin-3 (IL-3)dependent hematopoietic precursor cells (FDCP1) expressing a reporter plasmid that codes for herpes simplex virus-thymidine kinase, neomycin phosphotransferase, and murine IL-3 were transduced with a retroviral gene- ***trap*** ***vector*** carrying coding sequences for Cre-recombinase (Cre) in the U3 region. Activation of Cre expression from integrations into active genes resulted in a permanent switching between the selectable marker genes that converted the FDCP1 cells to factor independence. Selection for autonomous growth yielded recombinants in which Cre sequences in the U3 region were expressed from upstream

cellular promoters. Because the expression of the marker genes is independent of the trapped cellular promoter, genes could be identified that were transiently induced by IL-3 withdrawal.

=> s loxp (3a) muta?
L12 180 LOXP (3A) MUTA?

=> s l12 and vector
L13 36 L12 AND VECTOR

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 29 DUP REM L13 (7 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 29 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:864471 CAPLUS
TI A new combination of mutated loxPs in a ***vector*** for construction of phage antibody libraries
AU Gan, Yu; Zhao, Xin-Tai
CS Shanghai Medical College, Fudan University, Shanghai, 200032, Peop. Rep. China
SO Acta Biochimica et Biophysica Sinica (2005), 37(7), 495-500
CODEN: ABBSC2; ISSN: 1672-9145
PB Blackwell Publishing Asia Pty Ltd.
DT Journal
LA English
AB In the construction of large antibody libraries by in vivo recombination, two non-homogeneous loxP sites are required for the exchange of V genes between phagemids to create many new VH-VL combinations. The mutated loxP511 was designed not to recombine with the wild-type loxP (loxPwt) in early studies and a combination of the two has been used to construct antibody libraries. But recent reports have shown that recombination occurs between loxPwt and loxP511. This suggests that the combinational use of loxP511 and loxPwt might lead to the loss of the V gene diversity of antibody libraries. Therefore, it is necessary to find a new combination of loxPs to avoid the excision recombination in the antibody library. In this study, we found that the excision recombination between loxP511 and loxP2272, another ***mutated*** ***loxP*** sequence, was undetectable within one phagemid, while the excision recombination between loxP511 and loxPwt occurred at a frequency of 40%, higher than that reported previously. Furthermore, the in vivo recombination of different phagemids with loxP511 and loxP2272 showed that the V gene exchange was efficiently mediated to produce new VH-VL combinations. It was concluded that the loxP511 and loxP2272 combination was more favorable for reducing the excision recombination and constructing large phage antibody libraries with high diversity.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:419442 CAPLUS
DN 143:110288
TI Production of viral vectors using recombinase-mediated cassette exchange
AU Nakano, Masakazu; Odaka, Kazuhiko; Takahashi, Yuzuka; Ishimura, Masakazu;
Saito, Izumu; Kanegae, Yumi
CS Institute of Medical Science, Laboratory of Molecular Genetics, University of Tokyo, Minato-ku, Tokyo, 108-8639, Japan
SO Nucleic Acids Research (2005), 33(8), e76/1-e76/8
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB DNA viruses are often used as vectors for foreign gene expression, but large DNA region from cloned or authentic viral genomes must usually be handled to generate viral vectors. Here, we present a unique system for generating adenoviral vectors by directly substituting a gene of interest in a small transfected plasmid with a replaced gene in a replicating viral genome in Cre-expressing 293 cells using the recombinase-mediated cassette exchange (RMCE) reaction. In combination with a pos. selection of the viral cis-acting packaging signal connected with the gene of interest, the purpose ***vector*** was enriched to 97.5 and 99.8% after three and four cycles of infection, resp. Our results also showed that the ***mutant*** ***loxP*** V (previously called loxP 2272), a variant target of Cre used in the RMCE reaction, was useful as a non-compatible ***mutant*** to wild-type ***loxP*** . This method could be useful for generating not only a large no. of adenovirus vectors simultaneously, but also other DNA virus vectors including helper-dependent adenovirus ***vector*** .
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2005:322793 BIOSIS
DN PREV200510116530
TI Production of viral vectors using recombinase-mediated cassette exchange.
AU Nakano, Masakazu; Odaka, Kazuhiko; Takahashi, Yuzuka; Ishimura, Masakazu;
Saito, Izumu; Kanegae, Yumi [Reprint Author]
CS Kyoto Prefectural Univ Med, Dept Genom Med Sci, Kamigyo Ku, Kyoto 6028566,
Japan
kanegae@ims.u-tokyo.ac.jp
SO Nucleic Acids Research, (2005) Vol. 33, No. 8.
CODEN: NARHAD. ISSN: 0305-1048.
DT Article
LA English
ED Entered STN: 25 Aug 2005
Last Updated on STN: 25 Aug 2005
AB DNA viruses are often used as vectors for foreign gene expression, but large DNA region from cloned or authentic viral genomes must usually be handled to generate viral vectors. Here, we present a unique system for generating adenoviral vectors by directly substituting a gene of interest in a small transfected plasmid with a replaced gene in a replicating viral genome in Cre-expressing 293 cells using the recombinase-mediated cassette exchange (RMCE) reaction. In combination with a positive selection of the viral cis-acting packaging signal connected with the gene of interest, the purpose ***vector*** was enriched to 97.5 and 99.8% after three and four cycles of infection, respectively. Our results also showed that the ***mutant*** ***loxP*** V (previously called loxP 2272), a variant target of Cre used in the RMCE reaction, was useful as a non-compatible ***mutant*** to wild-type ***loxP*** . This method could be useful for generating not only a large number of adenovirus vectors simultaneously, but also other DNA virus vectors including helper-dependent adenovirus ***vector*** .

L14 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:589297 CAPLUS
DN 141:135211
TI Isolated N-cad+/CD45- osteoblasts which form niches that support hematopoietic stem cell (HSC), Bmpr1a-knocked-out mice containing the same, and uses thereby
IN Li, Linheng; Zhang, Jiwang
PA USA
SO U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004143863 | A1 | 20040722 | US 2003-641319 | 20030814 |
| WO 2004063341 | A2 | 20040729 | WO 2004-US415 | 20040109 |
| WO 2004063341 | A3 | 20050526 | | |

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRAI US 2003-439198P P 20030110
US 2003-641319 A 20030814
AB The present invention relates to an isolated population of osteoblastic cells, which form niches in vivo that support hematopoietic stem cell (HSC), and have a potential to be used as feeder cells to expand HSCs in vitro. In particular, the present invention relates to an isolated population of osteoblastic cells, which are characterized by cell surface markers N-cad + and CD45 -. The present invention also relates to methods for isolating the osteoblast population, as well as methods for supporting HSCs in vitro. Addnl., the present invention relates to vectors, which include a Bmpr1a (Alk3) nucleic acid sequence, recombination sites, and a plasmid, wherein the vectors can be used to promote an increase in the HSC population in vivo. The ***vector*** , preferably is an inducible Cre/Flp recombinase expression ***vector*** , whereby Bmpr1a ***mutant*** is flanked by ***LoxP*** sites. A knockout mouse, wherein the Bmpr1a gene has been substantially eliminated, was produced in order to investigate the roles of BMP signalling in regulating HSC development in vivo.

L14 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:327753 CAPLUS
DN 141:2013
TI A set of loxP marker cassettes for Cre-mediated multiple gene disruption in Schizosaccharomyces pombe
AU Iwaki, Tomoko; Takegawa, Kaoru
CS Department of Life Sciences, Faculty of Agriculture, Kagawa University, Kagawa, 761-0795, Japan
SO Bioscience, Biotechnology, and Biochemistry (2004), 68(3), 545-550
CODEN: BBBIEJ; ISSN: 0916-8451
PB Japan Society for Bioscience, Biotechnology, and Agrochemistry
DT Journal
LA English
AB For functional anal., the presence of gene families and isoenzymes often makes it necessary to delete more than one gene, while the no. of marker genes is limited in Schizosaccharomyces pombe. Here the authors describe a loxP-flanked ura4+ cassette and Cre recombinase ***vector*** for a Cre-loxP-mediated marker removal procedure in S. pombe. This loxP-ura4-loxP cassette can be used for disruption of hmt1+ as a model

target gene. The authors have constructed two vectors which express Cre recombinase under the control of the nmt1 or nmt41 promoter. Excisive recombination at loxP sites in the chromosome was promoted efficiently and accurately when the Cre recombinase was expressed under the control of the nmt41 promoter. In addn., ura4+ could be excised from the genome by Cre recombinase, when a single loxP site was adjacent to ura4. The use of the Cre-loxP system proved to be a practical strategy to excise a marker gene for repeated use in S. pombe.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:590189 CAPLUS
DN 141:326359
TI Conditional gene mutagenesis in B-lineage cells
AU Casola, Stefano
CS The CBR Institute for Biomedical Research, Harvard Medical School, Boston, MA, USA
SO Methods in Molecular Biology (Totowa, NJ, United States) (2004), 271(B Cell Protocols), 91-109
CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal
LA English
AB Since its first application in mice almost 10 yr ago, the Cre/loxP has become the system of choice to study gene function in vivo in a cell-type, stage-specific, and inducible manner. This chapter provides a set of updated protocols that will help the reader to construct a ***vector*** for conditional gene targeting, to in vitro manipulate embryonic stem (ES) cells and to rapidly identify successfully targeted ES colonies. It also provides an updated list of Cre strains currently used to assess gene function at defined stages of B-cell development and guidelines to generate single-copy, knock-in transgenes regulated in a Cre-dependent manner.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1
AN 2004:325715 BIOSIS
DN PREV200400327152
TI Separate control of Rep and Cap expression using ***mutant*** and wild-type ***loxP*** sequences and improved packaging system for adeno-associated virus ***vector*** production.
AU Mizukami, Hiroaki; Okada, Takashi; Ogasawara, Yoji; Matsushita, Takashi; Urabe, Masashi; Kume, Akihiro; Ozawa, Keiya [Reprint Author]
CS Ctr Mol MedDiv Genet Therapeut, Jichi Med Sch, 3311-1,Yakushiji, Minami Kawachi, Tochigi, 3290498, Japan
kozawa@ms2.jichi.ac.jp
SO Molecular Biotechnology, (May 2004) Vol. 27, No. 1, pp. 7-14. print.
ISSN: 1073-6085 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 29 Jul 2004
Last Updated on STN: 29 Jul 2004
AB Adeno-associated virus (AAV) vectors are a practical choice for gene transfer, and demand for them is increasing. To cope with the necessity in the near future, we have developed a number of approaches to establish packaging cell lines for the production of AAV vectors. In our previous study, a-highly regulated expression of large Rep proteins was obtained by using,the Cke-loxP. switching system. Therefore, in the present study, to regulate Cap expression as well, we developed an inducible expression system for both Rep and Cap proteins by using an additional set of ***mutant*** ***loxP*** sequences. The mutants possess two base alterations in the spacer region of loxP and recombine specifically with the same counterpart in the presence of Cre. By using two separate plasmids, one with mutant and the other with wild-type loxP sequences, the expression of two different proteins can be induced simultaneously by Cre recombinase. When the LacZ-encoding plasmid ***vector*** was used as a packaging model, a significant packaging titer of 2.1 x 1010 genome copies per 10-cm dish was obtained. These results indicate the importance of controlling Cap expression, in addition to Rep, to achieve an optimum production rate for AAV vectors.

L14 ANSWER 8 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:254918 BIOSIS
DN PREV200300254918
TI An improved PAC shuttle ***vector*** system for bidirectional deletion analysis.
AU Prasad, A. [Reprint Author]; Howell, K. [Reprint Author]; Coren, J. [Reprint Author]
CS Department of Biology, Elizabethtown College, Elizabethtown, PA, 17022, USA
SO Journal of the Pennsylvania Academy of Science, (March 2003) Vol. 76, No. Abstract and Index Issue, pp. 129-130. print.
Meeting Info.: 79th Annual Meeting of the Pennsylvania Academy of Science. Grantville, Pennsylvania, USA. April 04-06, 2003.
CODEN: JPSCEY. ISSN: 1044-6753.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 28 May 2003
Last Updated on STN: 28 May 2003

L14 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:539708 CAPLUS
DN 139:208462
TI Simultaneous on/off regulation of transgenes located on a mammalian chromosome with Cre-expressing adenovirus and a ***mutant*** ***loxP***
AU Kondo, Saki; Okuda, Aya; Sato, Hiromi; Tachikawa, Naoto; Terashima, Miho; Kanegae, Yumi; Saito, Izumu
CS Institute of Medical Science, Laboratory of Molecular Genetics, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo-8639, 108-8639, Japan
SO Nucleic Acids Research (2003), 31(14), e76/1-e76/10
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The site-specific recombinase Cre has often been used for on/off regulation of expression of transgenes introduced into the mammalian chromosome. However, this method is only applicable to the regulation of a single gene and cannot be used to simultaneously regulate two genes, because site-specific recombination occurs from the target loxP sequence of one regulating unit to the loxP sequence of any other unit and would eventually disrupt the structure of both regulating units. We previously reported a ***mutant*** ***loxP*** sequence with a two base substitution called loxP V (previously called loxP 2272), with which wild-type loxP cannot recombine but with which the identical ***mutant*** ***loxP*** recombines efficiently. In the present study we isolated cell lines bearing two regulating units on a chromosome contg. a pair of wild-type ***loxP*** sequences or ***mutant*** ***loxP*** V sequences. After infection with Cre-expressing recombinant adenovirus AxCANCre, expression of a gene in each regulating unit was simultaneously turned on and off. Southern analyses showed that both regulating units were processed simultaneously and independently, even after infection with a limited amt. of AxCANCre. The results showed that simultaneous regulation of gene expression on a mammalian chromosome mediated by Cre can be achieved by using ***mutant*** ***loxP*** V and wild-type loxP. This method may be a useful approach for conditional transgenic/knockout animals and investigation of gene function involving two genes simultaneously. Another possible application is for prepn. of a new packaging cell line of viral vectors through simultaneous prodn. of toxic viral genes.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:68628 BIOSIS
DN PREV200300068628
TI Methods for producing members of specific binding pairs.
AU Griffiths, Andrew David [Inventor, Reprint Author]; Williams, Samuel Cameron [Inventor]; Waterhouse, Peter Michael [Inventor]; Nissim, Ahuva [Inventor]; Winter, Gregory Paul [Inventor]; Johnson, Kevin Stuart [Inventor]; Smith, Andrew John Hammond [Inventor]
CS Cambridge, UK
ASSIGNEE: Cambridge Antibody Technology Limited, Cambridgeshire, UK; Medical Research Council, London, UK
PI US 6492160 20021210
SO Official Gazette of the United States Patent and Trademark Office Patents, (Dec 10 2002) Vol. 1265, No. 2. http://www.uspto.gov/web/menu/patdata.html . e-file.
ISSN: 0098-1133 (ISSN print).
DT Patent
LA English
ED Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003
AB Methods, recombinant host cells and kits are disclosed-for the production of members of specific binding pairs (sbp), e.g. antibodies, using display on the surface of secreted replicable genetic display packages (rgdps), e.g. filamentous phage. To produce a library of great diversity recombination occurs between first and second vectors comprising nucleic acid encoding first and second polypeptide chains of sbp members respectively, thereby producing recombinant vectors each encoding both a first and a second polypeptide chain component of a sbp member. The recombination may take place in vitro or intracellularly and may be site-specific, e.g. involving use of the ***loxP*** sequence and ***mutants*** thereof. Recombination may take place after prior screening or selecting for rgdps displaying sbp members which bind complementary sbp member of interest.

L14 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:924328 CAPLUS
DN 138:20472
TI Animal disease model with knockout von Hippel-Lindau disease gene and related gene targeting vectors
IN Schmidt, Laura S.; Ma, Wenbin; Tessarollo, Lino; Zbar, Berton
PA Department of Health and Human Services, USA

SO Statutory Invent. Regist., 20 pp.
CODEN: SRXXEV
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2056 | H1 | 20021203 | US 2001-971476 | 20011004 |

PRAI US 2001-971476 20011004
AB Disclosed herein are nucleic acid mols. that can be used to effect a loss of function of the von Hippel-Lindau (VHL) allele in somatic and/or germ cells of a mammal and methods for using these mols. to create conditional VHL gene targeted and conditional VHL knockout animals. Disclosed herein are conditional VHL gene target vectors which, when inserted into an endogenous VHL gene, can result in deletion of an exon of a VHL gene by site-specific recombination when a recombinase is expressed conditionally.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:970816 CAPLUS
DN 138:50870
TI Construction of trapping ***vector*** for preparation transgenic mouse with gene knocked out
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Kimi
PA Japan Science and Technology Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002369689 | A2 | 20021224 | JP 2001-157568 | 20010525 |

PRAI JP 2001-157568 20010525
AB The invention provides a process of construction of trapping ***vector*** for prepn. transgenic mouse with gene knocked out. The trapping ***vector*** consists of several patterns of combination of inverted repeating sequence, spacer, wild type and ***mutate*** ***loxP*** sequence. The invention also provides a DNA and encoding protein sequence of gene Ayu6003 trapped with by trapping ***vector*** which is sequence homolog of E. coli Ftsj gene. The invention also provided a transgenic mouse with Ayu6003 disrupted which can be used for drug screening.

L14 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:914707 CAPLUS
DN 138:12018
TI Vectors with ***mutated*** ***loxP*** sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Ide, Hiroyuki; Yamamura, Kenichi; Araki, Yoshimi
PA Japan Science and Technology Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2002345477 | A2 | 20021203 | JP 2001-157567 | 20010525 |

PRAI JP 2001-157567 20010525
AB Vectors for Cre-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The loxP sequence consisting of a inverted repeat sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, and having mutations in the inverted repeat sequence 1 or a inverted repeat sequence 2, is used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the ***vector*** into embryonic stem (ES) cells is claimed. Transgenic mice having disruptions in Tubedown-1 gene were generated from ES cells by introducing gene trap vectors of the invention.

L14 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:231876 CAPLUS
DN 137:227085
TI A Hoxa2 mutant conditional allele generated by Flp- and Cre-mediated recombination
AU Ren, Shu-Yue; Pasqualetti, Massimo; Dierich, Andree; Le Meur, Marianne; Rijli, Filippo M.
CS Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, College de France, Strasbourg, Fr.
SO Genesis (New York, NY, United States) (2002), 32(2), 105-108
CODEN: GNESFY; ISSN: 1526-954X
PB Wiley-Liss, Inc.
DT Journal
LA English
AB A Hoxa2 mutant allele suitable for efficient conditional knockout studies was generated using a 6.5 kb plasmid ***vector*** contg. the complete Hoxa2 gene and its flanking genomic sequences. A strategy based on Cre- and Flp-mediated recombination was employed to create a selection marker-free locus flanked by recombinase-specific sites. Neither the loxP sites nor the Frt-flanked phosphoglycerate kinase-neo cassette interrupted the Hoxa2 coding sequence.
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:833542 CAPLUS
DN 135:367645
TI Vectors with ***mutated*** ***loxP*** sequence and antisense promoter for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Taniguchi, Masaru; Karasawa, Mika
PA Japan Science and Technology Corporation, Japan
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001085973 | A1 | 20011115 | WO 2000-JP5824 | 20000829 |
| W: AU, CA, US | | | | |
| RW: DE, FR, GB, IT | | | | |
| JP 2001321174 | A2 | 20011120 | JP 2000-138938 | 20000511 |
| CA 2379095 | AA | 20011115 | CA 2000-2379095 | 20000829 |
| AU 2000067337 | A5 | 20011120 | AU 2000-67337 | 20000829 |
| EP 1281765 | A1 | 20030205 | EP 2000-955091 | 20000829 |
| R: DE, FR, GB, IT | | | | |

PRAI JP 2000-138938 A 20000511
WO 2000-JP5824 W 20000829
AB Vectors for Cre recombinase-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, antisense promoter transfer ***vector*** , and use in generation of embryonic stem cells (ES cells) having deficient expression of normal wild type genes, or gene knockout animals, are disclosed. The loxP sequence consisting of a inverted repeat sequence, lox71 or lox66, or FRT sequence, and spacer sequence, are used. Other genetic elements such as splicing acceptor or donor site, internal ribosomal entry site (IRES), marker gene, are also used. Reporter genes or selection marker genes such as neomycin resistance gene (neoR), puromycin resistance gene, hygromycin resistance gene, and diphtheria toxin gene, are used for ES cell prepn. Thymidine kinase gene or diphtheria toxin gene fused to phosphoglycero kinase gene promoter can be also used. A gene trap method comprising introducing the ***vector*** into embryonic stem (ES) cells is claimed. Gene knockout mice are claimed. By inserting a powerful promoter into a definite position in a mutated locus, wherein the insertion of the gene trap ***vector*** of the trapped clone has occurred, in the direction opposite to the endogenous gene, moreover, the antisense RNA against the trapped gene is compulsively transcribed and thus the transcription product from the wild type gene is disrupted.

L14 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:64171 CAPLUS
DN 134:126757
TI Vectors with ***mutated*** ***loxP*** sequence for Cre-mediated gene-trap-based insertional mutagenesis, and use in transgenic or gene knockout methods
IN Yamamura, Ken-ichi; Araki, Kimi
PA Transgenic Inc., Japan
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001005987 | A1 | 20010125 | WO 2000-JP2916 | 20000502 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2379055 | AA | 20010125 | CA 2000-2379055 | 20000502 |
| EP 1201759 | A1 | 20020502 | EP 2000-922969 | 20000502 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| AU 778719 | B2 | 20041216 | AU 2000-43176 | 20000502 |

PRAI JP 1999-200997 A 19990714
WO 2000-JP2916 W 20000502
AB Vectors for Cre-mediated gene trap insertional ***mutagenesis*** contg. a ***mutated*** ***loxP*** sequence, and use in generation of transgenic or gene knockout animals, are disclosed. The loxP sequence consisting of a reverse repetitive sequence 1, and spacer sequence and a reverse repetitive sequence 2 in this order, a mutation is transferred into a part of the reverse repetitive sequence 1 or a part of the reverse repetitive sequence 2. Other genetic elements such as splicing acceptor

or donor site, internal ribosomal entry site (IRES), marker gene, polyadenylation sequence, are also used. A gene trap method comprising introducing the ***vector*** into embryonic stem (ES) cells is claimed. Mouse, rat, rabbit, guinea pig, pig, sheep, or goat can be used as transgenic animals. Various gene trap vectors were constructed and introduced into ES cells. ES cell colonies contg. a single copy of the ***vector*** and retaining the lox71 sequence were selected by .beta.-gal marker gene expression. Transgenic mouse were generated.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:590614 CAPLUS
DN 136:211452
TI Isolation and subcloning of large fragments from BACs and PACs
AU Kaname, Tadashi; Huxley, Clare
CS Imperial College School of Medicine, London, SW7 2AZ, UK
SO BioTechniques (2001), 31(2), 273,276,278
CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton Publishing Co.
DT Journal
LA English
AB An improvement of the method using a mini-gel system with normal electrophoresis that is widely used in labs. is described. This modified method is simple, quick, and reliable for isolating large fragments from bacterial artificial chromosomes (BACs) and PI-derived artificial chromosomes (PACs). A new BAC ***vector*** , designated pBeloBAC66D1, which has a ***mutant*** ***loxP*** (lox66) and neomycin-resistant gene was constructed. To subclone a 155-kb insert of the human HPRT gene in a BAC into the new ***vector*** , 2.2 .mu.g BAC DNA was digested with NotI. The DNA fragments were then sepd. by electrophoresis through an agarose mini-gel and isolated by agarase treatment of the gel. The clones were checked by polymerase chain reaction targeted to the neomycin-resistant gene and to exon 9 of the human HPRT gene and by digestion with restriction enzymes followed by pulsed field gel electrophoresis. Of eight incorrect clones, five had only the self-ligated new ***vector*** , one had self-ligated pBeloBAC11, and two probably had no plasmids. The use of this improved protocol allowed a large fragment to be easily and efficiently subcloned into a new ***vector*** .
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:355971 BIOSIS
DN PREV200200355971
TI ***Mutant*** ***loxP*** vectors for selectable marker recycle and conditional knock-outs.
AU Arakawa, Hiroshi [Reprint author]; Lodygin, Dimitry; Buerstedde, Jean-Marie
CS Heinrich-Pette-Institute, Martinistrasse 52, D-20251, Hamburg, Germany hiroshi@genetics.hpi-uni-hamburg.de; lodyguin@biochem.mpg.de; buersted@genetics.hpi.uni-hamburg.de
SO BMC Biotechnology, (September 26, 2001) Vol. 1, No. 7 Cited May 5, 2002, pp. 1-8. http://www.biomedcentral.com/content/pdf/1472-6750-1-7.pdf. cited June 6, 2002. http://www.biomedcentral.com/1472-6750. online. ISSN: 1472-6750.
DT Article
LA English
ED Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002
AB Background: Gene disruption by targeted integration of transfected constructs becomes increasingly popular for studies of gene function. The chicken B cell line DT40 has been widely used as a model for gene knock-outs due to its high targeted integration activity. Disruption of multiple genes and complementation of the phenotypes is, however, restricted by the number of available selectable marker genes. It is therefore highly desirable to recycle the selectable markers using a site-specific recombination system like Cre/loxP. Results: We constructed three plasmid vectors (neoR, puroR and bsr), which carry selectable marker genes flanked by two different ***mutant*** ***loxP*** sites. After stable transfection, the marker genes can be excised from the genome by transient induction of Cre recombinase expression. This excision converts the two ***mutant*** ***loxP*** sites to an inactive double- ***mutant*** ***loxP*** . Furthermore we constructed a versatile expression ***vector*** to clone cDNA expression cassettes between ***mutant*** ***loxP*** sites. This ***vector*** can also be used to design knock-out constructs in which the floxed marker gene is combined with a cDNA expression cassette. This construct enables gene knock-out and complementation in a single step. Gene expression can subsequently be terminated by the Cre mediated deletion of the cDNA expression cassette. This strategy is powerful for analyzing essential genes, whose disruption brings lethality to the mutant cell. Conclusions: ***Mutant*** ***loxP*** vectors have been developed for the recycle of selectable markers and conditional gene knock-out approaches. As the marker and the cDNA expression cassettes are driven by the universally active and evolutionary conserved beta-actin promoter, they can be used for the selection of stable transfectants in a wide range of cell lines.

L14 ANSWER 19 OF 29 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2004278980 EMBASE
TI Mutants loxP vectors for selectable marker recycle and conditional knock-outs.
AU Arakawa H.; Lodygin D.; Buerstedde J.-M.
CS H. Arakawa, Heinrich-Pette-Institute, Martinistrasse 52, D-20251 Hamburg, Germany. hiroshi@genetics.hpi-uni-hamburg.de
SO BMC Biotechnology, (26 Sep 2001) Vol. 1, .
Refs: 16
ISSN: 1472-6750 CODEN: BBMIE6
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20040715
Last Updated on STN: 20040715
AB Background: Gene disruption by targeted integration of transfected constructs becomes increasingly popular for studies of gene function. The chicken B cell line DT40 has been widely used as a model for gene knock-outs due to its high targeted integration activity. Disruption of multiple genes and complementation of the phenotypes is, however, restricted by the number of available selectable marker genes. It is therefore highly desirable to recycle the selectable markers using a site-specific recombination system like Cre/loxP. Results: We constructed three plasmid vectors (neoR, puroR and bsr), which carry selectable marker genes flanked by two different ***mutant*** ***loxP*** sites. After stable transfection, the marker genes can be excised from the genome by transient induction of Cre recombinase expression. This excision converts the two ***mutant*** ***loxP*** sites to an inactive double- ***mutant*** ***loxP*** . Furthermore we constructed a versatile expression ***vector*** to clone cDNA expression cassettes between ***mutant*** ***loxP*** sites. This ***vector*** can also be used to design knock-out constructs in which the floxed marker gene is combined with a cDNA expression cassette. This construct enables gene knock-out and complementation in a single step. Gene expression can subsequently be terminated by the Cre mediated deletion of the cDNA expression cassette. This strategy is powerful for analyzing essential genes, whose disruption brings lethality to the mutant cell. Conclusions: ***Mutant*** ***loxP*** vectors have been developed for the recycle of selectable markers and conditional gene knock-out approaches. As the marker and the cDNA expression cassettes are driven by the universally active and evolutionary conserved .beta.-actin promoter, they can be used for the selection of stable transfectants in a wide range of cell lines.
.COPYRGT. 2001 Arakawa et al; licensee BioMed Central Ltd.

L14 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:804294 CAPLUS
DN 137:28709
TI ***Mutant*** ***loxP*** vectors for selectable marker recycle and conditional knock-outs
AU Arakawa, Hiroshi; Lodygin, Dimitry; Buerstedde, Jean-Marie
CS Heinrich-Pette-Institute, Hamburg, D-20251, Germany
SO BMC Biotechnology [online computer file] (2001), 1, No pp. given
CODEN: BBMIE6; ISSN: 1472-6750
URL: http://www.biomedcentral.com/content/pdf/1472-6750-1-7.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Gene disruption by targeted integration of transfected constructs is becoming increasingly popular for studies of gene function. The chicken B cell line DT40 has been widely used as a model for gene knock-outs due to its high targeted integration activity. Disruption of multiple genes and complementation of the phenotypes is, however, restricted by the no. of available selectable marker genes. It is therefore highly desirable to recycle the selectable markers using a site-specific recombination system like Cre/loxP. We constructed three plasmid vectors (neoR, puroR and bsr), which carry selectable marker genes flanked by two different ***mutant*** ***loxP*** sites. After stable transfection, the marker genes can be excised from the genome by transient induction of Cre recombinase expression. This excision converts the two ***mutant*** ***loxP*** sites to an inactive double- ***mutant*** ***loxP*** . Furthermore we constructed a versatile expression ***vector*** to clone cDNA expression cassettes between ***mutant*** ***loxP*** sites. This ***vector*** can also be used to design knock-out constructs in which the floxed marker gene is combined with a cDNA expression cassette. This construct enables gene knock-out and complementation in a single step. Gene expression can subsequently be terminated by the Cre-mediated deletion of the cDNA expression cassette. This strategy is powerful for analyzing essential genes, whose disruption brings lethality to the mutant cell. ***Mutant*** ***loxP*** vectors have been developed for recycling of selectable markers and conditional gene knock-out approaches. As the marker and the cDNA expression cassettes are driven by the universally active and evolutionary conserved .beta.-actin promoter, they can be used for the selection of stable transfectants in a wide range of cell lines.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:368560 CAPLUS
DN 133:13377
TI Methods for the preparation of nucleic acid and polypeptide libraries
IN Bradbury, Andrew Raymon Morton; Sblattero, Daniele
PA S.I.S.S.A. Scuola Internazionale Superiore Di Studi Avanzati, Italy
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000031246 | A2 | 20000602 | WO 1999-EP8856 | 19991118 |
| WO 2000031246 | A3 | 20000817 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| IT 1303776 | B1 | 20010223 | IT 1998-MI2509 | 19981119 |
| IT 98MI2509 | A1 | 20000519 | | |
| CA 2350779 | AA | 20000602 | CA 1999-2350779 | 19991118 |
| AU 2000037903 | A5 | 20000613 | AU 2000-37903 | 19991118 |
| EP 1131421 | A2 | 20010912 | EP 1999-972677 | 19991118 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI IT 1998-MI2509 A 19981119
WO 1999-EP8856 W 19991118
AB This invention provides novel methods of generating large, highly diverse, nucleic acid (and hence polypeptide) libraries. The methods exploit the discovery that recombination, particularly recombinase recombination can occur between two or more constructs of the same type (e.g. having the same origin of replication and/or the same regulatory or selectable markers). The methods thus involve introducing at least two members of an initial population of nucleic acid mols. into at least one cell under conditions where recombination (e.g recombinase-mediated recombination) can occur between the nucleic acids. The nucleic acid mols. preferably comprise two or more individual nucleic acids each of which consists of a nucleic acid sequence that is identical for each mol. and that includes an origin of replication; and a nucleic acid sequence that varies between members of said population. One preferred pair of recombination recognition sites is ***loxP*** and a ***loxP*** ***mutant*** (e.g., ***loxP*** 511 or fas loxP). A preferred library member is illustrated by the ***vector*** pDANS, which consists of an origin of replication, ampicillin resistance, a secretory leader, the tags (SV5 and His), gene 3, and the Ff origin of replication. In the example provided, there are two "variable" sequences that encode resp. a VH and a VL region of a single-chain antibody. Thus, a single type of construct is capable of mediating all of the recombination events, providing substantially greater efficiency and the creation of substantially larger and more diverse nucleic acid libraries.

L14 ANSWER 22 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN
AN 2001:17189 BIOSIS
DN PREV200100017189
TI Site-specific and directional gene replacement mediated by Cre recombinase.
AU Trinh, K. Ryan; Morrison, Sherie L. [Reprint author]
CS Department of Microbiology and Molecular Genetics, University of California, Los Angeles, CA, 90095-1747, USA
sheriem@microbio.ucla.edu
SO Journal of Immunological Methods, (20 October, 2000) Vol. 244, No. 1-2, pp. 185-193. print.
CODEN: JIMMBG. ISSN: 0022-1759.
DT Article
LA English
ED Entered STN: 27 Dec 2000
Last Updated on STN: 27 Dec 2000
AB A novel method for the site-specific introduction of genes into eukaryotic cells using the prokaryotic Cre-LoxP recombination system is presented. Cre recombinase catalyzes recombination between two LoxP sites or between two ***mutant*** ***LoxP*** 511 sites. However, recombination is not catalyzed between a LoxP and a LoxP 511 site. We now demonstrate that it is possible to catalyze accurate exchange between two DNA segments each flanked by a LoxP and a LoxP 511 site. In the example presented, expression of the Cre recombinase resulted in the replacement of a murine IgA constant region gene with a LoxP site at the 5' end and a LoxP 511 site at the 3' end by a human IgA constant region gene flanked by the same wild type and ***mutant*** ***LoxP*** sites. This method provides a novel approach for the site-specific substitution of specific genes.

L14 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:604982 CAPLUS
DN 129:185089
TI Method of constructing vectors for homologous recombination directed mutagenesis
IN Nehls, Michael; Wattler, Sigrid
PA USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9837175 | A1 | 19980827 | WO 1998-US3243 | 19980220 |

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

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|---|---|---|---|---|
| EP 912722 | A1 | 19990506 | EP 1998-908603 | 19980220 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

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|---|---|---|---|---|
| JP 2002514072 | T2 | 20020514 | JP 1998-536875 | 19980220 |
| US 6924146 | B1 | 20050802 | US 1998-171642 | 19980220 |
| US 2004043487 | A1 | 20040304 | US 2003-636822 | 20030806 |

PRAI DE 1997-19707012 A 19970221
US 1998-171642 A1 19980220
WO 1998-US3243 W 19980220
AB The present invention provides a novel ***vector*** system and thereby a novel method for the simplified construction of recombinant vectors for directed mutagenesis. A particularly useful ***vector*** class includes a linear lambda ***vector*** (lambdaKOS, i.e., knockout shuttle) that comprises: a stuffer fragment; an Escherichia coli origin of replication; an antibiotic resistance gene; a yeast origin of replication, a selectable marker suitable for use in yeast; a neg. selectable marker suitable for use in mammalian cells; and LoxP sequences for Cre recombinase-directed conversion of the linear lambda phage ***vector*** into an E. coli/yeast shuttle plasmid. An addnl. ***vector*** is designed to specifically insert a pos. selection cassette into cloned genomic DNA. Said ***vector*** system is used to modify the eukaryotic genome, particularly of embryonic stem cells, at precise and predefined loci by the means of homologous recombination. Furthermore, said system finds its usage in the generation of new strategies for gene therapy and in the generation of genetically modified higher eukaryotic organisms. The new method reduces the time required for the construction of such vectors from 3-6 mo to about 14 days.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 24 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN
AN 1998:446923 BIOSIS
DN PREV199800446923
TI A chimeric Cre recombinase inducible by synthetic, but not by natural ligands of the glucocorticoid receptor.
AU Brocard, Jacques; Feil, Robert; Chambon, Pierre [Reprint author]; Metzger, Daniel
CS Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, College de France, BP 163, C.U. de Strasbourg, 67404 Illkirch Cedex, France
SO Nucleic Acids Research, (Sept. 1, 1998) Vol. 26, No. 17, pp. 4086-4090. print.
CODEN: NARHAD. ISSN: 0305-1048.
DT Article
LA English
ED Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
AB We have developed a new ligand-dependent chimeric recombinase (Cre-GRdex)
by fusing the site-specific Cre recombinase to the ligand binding domain (LBD) of a mutant human glucocorticoid receptor (GRdex). The synthetic glucocorticoid receptor (GR) ligands dexamethasone, triamcinolone acetonide and RU38486 efficiently induce recombinase activity in F9 murine embryonal carcinoma cells expressing constitutively Cre-GRdex. In contrast, no recombinase activity was detected in the absence of ligand or in the presence of the natural GR ligands corticosterone, cortisol or aldosterone. Moreover, physiological concentrations of these natural GR ligands do not affect Cre-GRdex recombinase activity induced by dexamethasone. Thus, ,as previously shown using Cre-oestrogen receptor (ER) fusion proteins, Cre-GRdex might be useful for achieving ***loxP*** site-directed ***mutagenesis*** in cultured cells and spatio-temporally controlled somatic cell mutagenesis in transgenic mice.

L14 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:265521 CAPLUS
DN 129:36929
TI Selective disruption of genes transiently induced in differentiating mouse embryonic stem cells by using gene trap mutagenesis and site-specific recombination
AU Thorey, Irmgard S.; Muth, Katrin; Russ, Andreas P.; Otte, Jurgen; Reffelmann, Armin; Von Melchner, Harald
CS Laboratory for Molecular Hematology, Department of Hematology, University of Frankfurt Medical School, Frankfurt Am Main, 60590, Germany
SO Molecular and Cellular Biology (1998), 18(5), 3081-3088
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB A strategy employing gene trap mutagenesis and site-specific recombination

(Cre/loxP) has been used to identify genes that are transiently expressed during early mouse development. Embryonic stem cells expressing a reporter plasmid that codes for neomycin phosphotransferase and Escherichia coli LacZ were infected with a retroviral gene trap ***vector*** (U3Cre) carrying coding sequences for Cre recombinase (Cre) in the U3 region. Activation of Cre expression from integrations into active genes resulted in a permanent switching between the two selectable marker genes and consequently the expression of .beta.-galactosidase (.beta.-Gal). As a result, clones in which U3Cre had disrupted genes that were only transiently expressed could be selected. Moreover, U3Cre-activating cells acquired a cell autonomous marker that could be traced to cells and tissues of the developing embryo. Thus, when two of the clones with inducible U3Cre integrations were passaged in the germ line, they generated spatial patterns of .beta.-Gal expression.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 29 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 2
AN 97213953 EMBASE
DN 1997213953
TI Targeted integration of DNA using mutant lox sites in embryonic stem cells.
AU Araki K.; Araki M.; Yamamura K.-I.
CS K.-I. Yamamura, Department of Developmental Genetics, Inst Molecular Embryology Genetics, Kumamoto University School Medicine, Kumamoto 862, Japan. yamamura@gpo.kumamoto-u.ac.jp
SO Nucleic Acids Research, (1997) Vol. 25, No. 4, pp. 868-872.
Refs: 16
ISSN: 0305-1048 CODEN: NARHAD
CY United Kingdom
DT Journal; Article
FS 022 Human Genetics
LA English
SL English
ED Entered STN: 970807
Last Updated on STN: 970807
AB Site-directed DNA integration has been achieved by using a pair of mutant lox sites, a right element (RE) mutant lox site and a left element (LE) mutant lox site in mouse embryonic stem (ES) cells. We established ES cell lines carrying a single copy of the wild-type ***loxP*** or LE ***mutant*** lox site as a target and examined the frequency of site-specific integration of a targeting ***vector*** carrying a ***loxP*** or RE ***mutant*** lox site induced by Cre transient expression. Since our targeting ***vector*** contains a complete neo gene, random integrants can form colonies as in the case of a gene targeting event through homologous recombination. With our system, the frequency of site-specific integration via the mutant lox sites reached a maximum of 16%. In contrast, the wild-type loxP sites yielded very low frequencies (< 0.5%) of site-specific integration events. This mutated lox system will be useful for 'knock-in' integration of DNA in ES cells.

L14 ANSWER 27 OF 29 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 3
AN 96353962 EMBASE
DN 1996353962
TI Rapid construction in yeast of complex targeting vectors for gene manipulation in the mouse.
AU Storck T.; Kruth U.; Kolhekar R.; Sprengel R.; Seeburg P.H.
CS Center for Molecular Biology, University of Heidelberg, INF 282 Max-Planck Inst Medical Res, Jahnstrasse 29,69120 Heidelberg, Germany
SO Nucleic Acids Research, (1996) Vol. 24, No. 22, pp. 4594-4595.
ISSN: 0305-1048 CODEN: NARHAD
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 961210
Last Updated on STN: 961210
AB Targeting vectors for embryonic stem (ES) cells typically contain a mouse gene segment of > 7 kb with the neo gene inserted for positive selection of the targeting event. More complex targeting vectors carry additional genetic elements (e.g. lacZ, ***loxP*** , point ***mutations*** ). Here we use homologous recombination in yeast to construct targeting vectors for the incorporation of genetic elements (GEs) into mouse genes. The precise insertion of GEs into any position of a mouse gene segment cloned in an Escherichia coli/yeast shuttle ***vector*** is directed by short recombinogenic arms (RAs) flanking the GEs. In this way, complex targeting vectors can be engineered with considerable ease and speed, obviating extensive gene mapping in search for suitable restriction sites.

L14 ANSWER 28 OF 29 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4
AN 96001662 EMBASE
DN 1996001662
TI An antibody VH domain with a lox-Cre site integrated into its coding region: Bacterial recombination within a single polypeptide chain.
AU Davies J.; Riechmann L.
CS MRC Laboratory of Molecular Biology, Hills Road,Cambridge CB2 2QH, United Kingdom
SO FEBS Letters, (1995) Vol. 377, No. 1, pp. 92-96.
ISSN: 0014-5793 CODEN: FEBLAL
CY Netherlands
DT Journal; Article
FS 004 Microbiology
LA English
SL English
ED Entered STN: 960127
Last Updated on STN: 960127
AB Bacterial lox-Cre recombination within a single antibody VH domain was achieved through integration of a loxP site into its coding sequence. The 5' half of the VH gene, in which the H2 loop was replaced by a ***mutant*** ***loxP*** site, was fused to geneIII in an 'acceptor' fd-phage ***vector*** containing also a wild type loxP site. With a 'donor' plasmid ***vector*** harbouring the 3' half of the VH gene flanked by the same, differing loxP sites it recombined into a full-length VH with the loxP site-H2 loop. This VH was purified from bacterial periplasm, where it folded into a typical immunoglobulin domain. The system allows the generation of large VH repertoires using lox-Cre recombination.

L14 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:442218 CAPLUS
DN 119:42218
TI Combinatorial infection and in vivo recombination: A strategy for making large phage antibody repertories
AU Waterhouse, Peter; Griffiths, Andrew D.; Johnson, Kevin S.; Winter, Greg
CS Cent. Protein Eng., MRC, Cambridge, CB2 2QH, UK
SO Nucleic Acids Research (1993), 21(9), 2265-6
CODEN: NARHAD; ISSN: 0305-1048
DT Journal
LA English
AB An acceptor phage ***vector*** , fdDOG-2lox, and a donor plasmid ***vector*** , pUC19-2lox, utilizing the lox-Cre recombination system, were constructed for combinatorial infection of Escherichia coli to increase phage antibody repertories. The phage ***vector*** encodes the light chain variable region of one antibody and the heavy chain variable region of a 2nd, different, antibody; the plasmid ***vector*** encodes the heavy chain of the 1st antibody. In both vectors the heavy chain variable region genes were flanked by one wild-type and one ***mutant*** ***loxP*** sites. When Cre recombinase is provided in vivo by infection of E. coli with phage P1Cm c1.100, the two vectors can co-integrate by recombination between either ***mutant*** or wild-type ***loxP*** sites to create chimeric plasmids. Use of this system produced recombinant vectors that produced functional anti-2-phenyloxazol-5-one Fab fragments displayed on phage particles.

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FULL ESTIMATED COST 227.55 227.76

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